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JUL 76 R ANSBACHER, R G PARRISH

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CLINICAL INVESTIGATION SERVICE

Annual Research Progress Report

FISCAL YEAR 1976

Brooke Army Medical Center
Fort Sam Houston, Texas 78234

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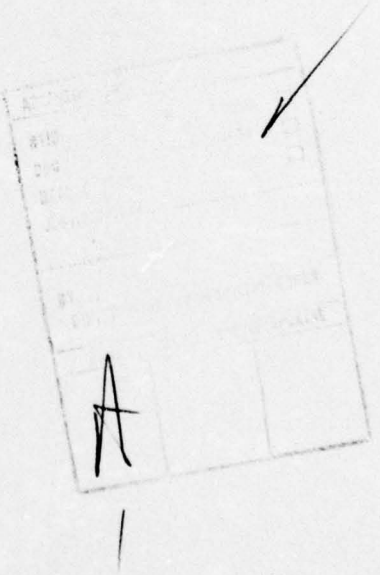

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FOREWORD

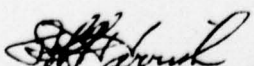
Fiscal year 1976 was one of growth and recognition for the Clinical Investigation Service. In addition to the Chief, Biochemist/Laboratory Director, and Physiologist, the Clinical Investigation Service is now authorized a Microbiologist and a Biomedical Information Systems Officer. The Biochemist continues to serve as Chief. The Physiologist reported in December 1975, and the Microbiologist is due to report in July 1976. The physiologist, with training in biomedical engineering and statistics, has greatly enhanced the CIS capability of analyzing scientific data. The microbiologist, with experience in radio-immunoassay, is also expected to contribute to the service's capabilities to support clinical investigations at Brooke Army Medical Center.

In FY 76 Clinical Investigation Service sponsored research received recognition at the 11th Annual Uniformed Services Pediatrics Seminar when Dr. Russell Steele, LTC, MC, Department of Pediatrics, received the Eighth Ogden Bruton Award for his work on BAMC approved protocol C-14-74. The Raymond Franklin Metcalfe Award was given to Dr. Daniel R. Bailey, MAJ, MC, Department of Surgery, for his work on BAMC approved protocol C-17-74. Both of these awards recognize and emphasize the high quality of research conducted at Brooke Army Medical Center.

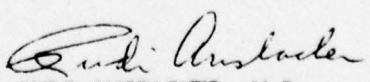
The number of manuscripts received in FY 76 fell to 80, 14 less than in FY 75, and the number of presentations fell from 60 in FY 75 to 25 in FY 76, the latter because of the shortage of TDY funds. The entire clinical investigational effort suffered from a shortage of consumable supply funds. Although consumable supply monies increased by $4,380.00 (excluding contractural services), this was blunted by the tremendous rise in the cost of scientific equipment and supplies.

FY 76 marked the completion of the first five years of the Clinical Investigation Service at Brooke Army Medical Center. The Service has grown from a total strength of two in 1971 to an authorized strength of 14, and this year assumed control of the Infectious Disease Laboratory. In the next five years, the Service plans to increase its complement of scientific equipment and the skill level of its technicians. Both these improvements will lead to increased effectiveness in supporting clinical investigation at Brooke Army Medical Center, and both depend on the continued support of the Hospital Commander, his administrative staff, and the professional medical staff.

This report and the efficient management of the multitude of administrative tasks in the Clinical Investigation Service would not be possible without the devoted and unselfish support of Mrs. Dodie Bratten to whom we express our most sincere appreciation.



ROB G. PARRISH, Ph.D.
Captain, MSC
Chief, Clinical Investigation Service



RUDI ANSBACHER, M.D.
Colonel, MC
Chairman, Directorate for Clinical Investigation Service

REPORT OF TOTAL ACTIVITIES OF CLINICAL INVESTIGATION SERVICE

DURING FISCAL YEAR 1976

A. Objectives

The Clinical Investigation Service was established at Brooke Army Medical Center 9 August 1971 to coordinate clinical investigation activities throughout the hospital complex. It is an independent service directly under the command of the Director of Medical Education, and operates under the guidance of the Directorate for Clinical Investigations, composed of three members from the Department of Medicine and one each from Obstetrics-Gynecology, Pediatrics, and Surgery; the Clinical Investigation Committee, composed of the chiefs of the various professional departments; and the Human Use Committee, composed of lay personnel.

The Clinical Investigation Service was established to promote, stimulate, coordinate, and provide support for clinical investigation and development activities within Brooke Army Medical Center, including design of experiments, typing and editorial services, and technical liaison with outside facilities.

B. Technical Approach

		Manpower	
Name	Rank	Authorized	Title
	LTC	03139	Chief
Parrish, Rob G.	CPT	03309	Biochemist
Giolma, John P.	CPT	03327	Physiologist
	CPT	03307	Microbiologist
		03520	Biomedical Information Systems Officer
Selfridge, Hartley A.	SP6	92B30	Sr Med Lab Sp, NCOIC
	SP6	92B30	Sr Med Lab Sp
Breen, Robin	SP5	92B20	Med Lab Sp
Sosa, Raul	SP4	92B20	Med Lab Sp
Plant, Harris D.	SP4	92B20	Med Lab Sp
Andruss, Theodore	SP4	92B20	Med Lab Sp
Quagliani, Joseph	SP3	92B20	Med Lab Asst
Bratten, Dodie	GS6		Editorial Assistant

Directorate for Clinical Investigation Service

Name	Rank	Organization	Title
Ansbacher, Rudi	COL	Department of Obstetrics and Gynecology	Chairman
Parrish, Rob G.	CPT	Clinical Investigation Service	Recorder
Zeigler, Michael G.	COL	Department of Surgery	Member
Murgo, Joseph P.	LTC	Department of Medicine	Member
Bowman, Robert P.	LTC	Department of Medicine	Member
McNitt, Theodore R.	LTC	Department of Medicine	Member
Steele, Russell W.	LTC	Department of Pediatrics	Member

	Funding FY 76	
MEDCASE	$ 71,494.00	6 Protocols
	$ 28,656.00	Laboratory
	$100,150.00	
Capital Equipment	$ 930.00	1 Protocol
	$ 2,386.50	Laboratory
	$ 3,316.50	
Consumable Supplies	$ 21,818.00	23 Protocols
	$ 12,142.00	Laboratory
	$ 9,340.00	Contractural Services
	$ 43,300.00	
TDY*	$ 288.00	
TOTAL	$147,054.50	

*The Clinical Investigation Service was not allocated TDY funds to support travel in conjunction with approved protocols.

C. Progress

Protocol Disposition FY 76*

	Completed	Terminated	Ongoing to FY 77
FY 72	1	0	3
FY 73	0	0	2
FY 74	8	4	10
FY 75	10	4	15
FY 76	2	2	32
	21	10	62

*See Annual Report, FY 75, for protocols ongoing to FY 76.

During FY 76, 80 manuscripts were cleared through the Clinical Investigation Service, 40 for publication, 20 for satisfaction of residency requirement and 20 both for satisfying residency requirement and for publication. Twenty-five presentations were reviewed and cleared by the Clinical Investigation Service for national and international medical meetings, and most of the material came from protocols registered in the Clinical Investigation Service. Thirty-five manuscripts emanating from Clinical Investigation Service sponsored projects have been published in national journals during FY 76.

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Brooke Army Medical Center
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Lubensky, J.D. The case against the crooked penis. Presented at the Western Section, American Urological Association, Inc., San Diego, Calif-, Feb. 1976.

PHARMACY SERVICE

Salter, C.S., Winship, H.W., III and Trinca, C.E. The clinical pharmacist as applied pharmacologist assisting the clinical pharmacologist in influencing pediatric therapy. J. Amer. Soc. Hosp. Pharm. (In Press).

Salter, C.S. The clinical pharmacist as applied pharmcologist assisting the clinical pharmacologist in influencing pediatric therapy. Presented at the American Society of Hospital Pharmacists Tenth Annual Meeting, 7-11 Dec 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

AWARDS

C-14-74. Evaluation of Cellular Immunity to the Varicella-Zoster Virus Employing a Newly Developed Microassay Technique.

Principal Investigator: LTC Russell W. Steele
Department of Pediatrics

Eighth Ogden Bruton Award.

C-17-74. The Effect of Cardiopulmonary Bypass on the Renin-Angiotensin System.

Principal Investigator: MAJ Daniel R. Bailey
Department of Surgery

Raymond Franklin Metcalfe Award.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Human Hepatic *in vitro* Metabolism of the Synthetic and Natural Estrogens.

WORK UNIT NO.: C-1-75

PRINCIPAL INVESTIGATOR: Edward D. Helton, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To correlate the *in vivo* metabolism of 17α-ethynylestradiol and estradiol to the *in vitro* hepatic metabolism and to establish what hepatotoxic effects the potent synthetic estrogen may have upon normal liver function.

TECHNICAL APPROACH

The *in vivo* metabolism of 17α-ethynylestradiol (EE_2) was studied in castrate and normal women through collaboration with Joseph W. Goldzieher, M.D. and Mary C. Williams at the Southwest Foundation for Research and Education, San Antonio. *In vitro* studies were completed in the baboon and human liver. Human tissue slices were incubated with hormone; whereas, baboon liver microsomes were isolated for incubation. The radiolabeled products from all experiments were purified and identified through columnar (lipophilic Sephadex), reverse isotope dilution and gas liquid chromatography-mass spectrometery.

Manpower: 1 SP4 (8 months)
1 SP4 (4 months)

Funding:	FY 1976	FY 1975
Consumable Supplies	$771.57	$2,260.16
TDY	$236.00	$ 288.00

PROGRESS

A comparison of the *in vivo* metabolism and *in vitro* alterations of EE_2 by human liver was made and significant quantitative differences were observed

C-1-75 (continued)

suggesting the primary glucuronide conjugate in humans may not be formed in the liver. The principal in vivo conjugate was tentatively identified as the 3-β-D-glucopyranosiduronate. The in vivo and in vitro variations in conjugation was also studied and significant differences were apparent among individuals. Baboon liver microsomes were found to de-ethynylate EE_2, and the reaction was indicated to be oxidative.

Status: Completed.

Helton, E.D., Williams, M.C. and Goldzieher, J.W. Human urinary and liver conjugates of 17α-ethynylestradiol. Steroids, June 1976.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Some Common Dietary Constituents on the Solubility of Cholesterol in Lipid Bilayer Membranes.

WORK UNIT NO.: C-24-76

PRINCIPAL INVESTIGATOR: Rob G. Parrish, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if xanthine oxidase, polyunsaturated fatty acids, or other lipophilic or lipo-active dietary constituents might affect cholesterol solubility in lipid bilayer membranes and thus play a role in the etiology of atherosclerosis.

TECHNICAL APPROACH

As outlined in the original protocol, the technical approach consists of three phases. Phase 1 is extraction of lipids necessary for the experiments; phase 2 is construction of a heating block suitable for mounting on a microscope stage; and phase 3 will use the heating block to determine the phase diagrams of lecithin and lysolecithin-cholesterol layer. Due to difficulties encountered in phase 2, the method of detecting phase changes in phase 3 may have to be modified. The changes will involve the use of more sensitive methods of detecting phase changes in lipid bilayer membranes. Specifically, electron microscopy and electron spin resonance. Arrangements for the use of these two techniques are being made at the present time.

Manpower: 1 SP4 (3 months)

Funding: FY 1976

Consumable Supplies	$1,817.77

PROGRESS

Phase 1 has been completed and some preliminary experiments have been performed using the phase contrast microscope. Gross phase changes

C-24-76 (continued)

can be detected. However, to detect small crystal aggregates of free cholesterol it may be necessary to use other techniques, specified above. The initial version of the heating block for the microscope has been constructed and was not adequate for the experiments outlined because the machine shop did not adhere to specified dimensions. Another block is now being constructed.

Status: Ongoing

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Investigation of the Effect of CNS Active Drugs on Membrane Bound Cations.

WORK UNIT NO.: C-28-76

PRINCIPAL INVESTIGATOR: Rob G. Parrish, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATOR: Robert L. Watson, Jr., M.D., LTC, MC

OBJECTIVES

To better understand the effect of CNS depressants and narcotic antagonists on sodium and calcium bound to nerve membranes, and to develop a safe and efficient *in vitro* method of evaluating the potency of narcotics and narcotic antagonists.

TECHNICAL APPROACH

Calcium and sodium are both known to bind to phosphatidyl serine (PS) a major constituent of neural tissue. Cephalin fraction, which contains PS, has been extracted from bovine brain and several grams of pure PS has been separated from the cephalin fraction. The second phase of the research is to measure the binding of soium and calcium to lipid bilayer membranes. The original protocol calls for the use of radioactive sodium-22 and calcium-44 which are both gamma emitters. Use of these nucleotides is waiting the completion of the isotope work area in the Clinical Investigation Laboratory. In the meantime, a sensitive method utilizing fluorometric methods has been adopted to determine calcium concentrations in the ppm range and preliminary experiments have been conducted using this technique.

Manpower: 1 SP4 (2 months)

Funding: None.

PROGRESS

Over $2,000.00 worth of pure lipids have been extracted using less than one-tenth that amount in materials. As mentioned above, preliminary

C-28-76 (continued)

experiments have been performed using fluorometric methods to detect binding of calcium to PS in lipid bilayer membranes. Binding of the divalent cation can be detected and the next step is the addition of anesthetic in the experiment.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Correlation of the Molecular Conformation of Erythromycin 2'Esters and Bioactivity.

WORK UNIT NO.: C-34-76

PRINCIPAL INVESTIGATORS: Dennis L. Stevens, M.D., MAJ, MC
Rob G. Parrish, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the nuclear magnetic resonance of various erythromycin 2'esters in order to predict the feasibility of developing better drugs for clinical use.

TECHNICAL APPROACH

Erythromycin is administered as the ester of a variety of fatty acids covalently bound to the 2' position. The biological activity and toxicity of these esters has been established, however, the subtlety of the substitutions does not suggest the wide range of response obtained from administering the different esters.

Nuclear magnetic resonance techniques will be used to determine the conformation of several esters of erythromycin as a function of pH. Specifically, we will measure the Spin Lattice relaxation times (T_1's) of different functional groups in the molecule. We will correlate the conformational changes with intestinal absorption, antibiotic potency, and hepatic toxicity reported in the literature. Ideally, the *in vitro* data we collect, coupled with the physiological data found in the literature will enable us to choose an ester which will yield an intermediate conformational change and will retain the qualities necessary for effective clinical use.

Manpower: None.

Funding: None.

C-34-76 (continued)

PROGRESS

This is a new project.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Oral Transplants of Freeze-Dried Allografts.

WORK UNIT NO.: C-12-75

PRINCIPAL INVESTIGATOR: John H. Moyer, D.D., MAJ, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine whether freeze-dried bone allografts can be used in one, two, and combined one and two wall oral bony defects with predictable results.

TECHNICAL APPROACH

The surgical site is exposed via a buccal and lingual full or partial thickness mucoperiosteal flap. Intraosseous defects are recontoured and one wall or two wall bony defects are prepared by removing the cortical plate within the defect. The freeze-dried allograft material is mixed with sterile saline to a paste-like consistency and packed in and around the existing bony defect. The patients will be recalled one year post-grafting to re-open the operative site for evaluation and additional surgical intervention as indicated.

Manpower: None.

Funding: None.

PROGRESS

To date thirteen individuals have been treated as described above. One graft was used for twelve people while one person received three different grafts. Eight patients have completed the one year follow-up re-entry.

C-12-75 (continued)

Four patients remain to be completed and one individual moved away from this area. We have yet to find any evidence of osseous regeneration.

Status: Ongoing.

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Design Alterations upon Abutment Tooth Mobility with Removable Partial Dentures.

WORK UNIT NO.: C-28-75

PRINCIPAL INVESTIGATOR: John McCartney, D.D.S., MAJ, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine via intraoral procedures whether alterations in design of the prosthesis have any effect upon the amount and direction of force transmitted to the abutment tooth when a bilateral extension removable partial denture is subjected to forces upon its distal extension bases.

TECHNICAL APPROACH

A bilateral distal extension removable partial denture was made abutting with teeth #21 and 27. Teeth #21 and 27 will receive restoration via full crown castings. The partial denture will have five removable components to allow for variation of clasping and comparisons of transmitted forces to abutments. Tooth #21 will serve as the test abutment. Movements buccolingually and mesiodistally are to be measured by pressure gauges attached to a fixed platform attached to teeth #23-26. Alterations in the master framework will give information as to the relative influence of its component parts.

Manpower: None.

Funding: None.

PROGRESS

Project terminated due to PCS of principal investigator.

Status: Terminated.

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Enflurane (Ethrane) as an Amnesic Analgesic for Outpatient Oral Surgery.

WORK UNIT NO.: C-20-76

PRINCIPAL INVESTIGATOR: Richard A. Kraut, D.D.S., MAJ, DC

ASSOCIATE INVESTIGATORS: Robert L. Watson, M.D., LTC, MC; Alejandro Acevedo, D.D.S., COL, DC

OBJECTIVES

1. To determine the feasibility of using Enflurane to create a state of cooperative amnesia for outpatient oral surgery.
2. To determine the concentration of Enflurane required to create a state of cooperative analgesia and the level of amnesia associated with that state.
3. To assess the length of recovery time needed after the administration of Enflurane as an amnesic agent, before patients can be sent home in the care of a responsible adult.

TECHNICAL APPROACH

Fifty patients will be selected from those presenting to the Oral Surgery Clinic requiring general anesthesia for surgical removal of impacted teeth or multiple extractions. The week prior to the procedure a history and physical will be accomplished. While in the Oral Surgery Clinic waiting room, a psychomotor function test will be administered. The patient will be seated in a contour dental chair and an intravenous infusion of D_5RL started and maintained until the patient is recovered from the analgesic effect of Enflurane. The following monitors will be used: ECG, pneumotachygraph and nasal thermistor to indicate rate and depth of respiration, blood pressure via an Arteriosonde; precordial stethoscope. Oxygen will be administered and enflurane gradually added to O_2 to achieve a state of cooperative analgesia. Following the surgical procedure, the patient's recovery from Enflurane will be assessed utilizing the same psychomotor function test administered previously. Once psychomotor function and cardiopulmonary parameters have returned to preanalgesic levels, the patients will be discharged home.

Manpower: None.

Funding: FY 1976

MEDCASE $10,200.00

C-20-76 (continued)

PROGRESS

It is anticipated the study will begin 1 July 1976.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Study of the Effects of Taper, Preparation Height, and Axial Grooves upon Resistance Form of Full Crown Preparation.

WORK UNIT NO.: C-31-76

PRINCIPAL INVESTIGATOR: Gerald D. Woolsey, D.D., MAJ, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the relative resistance to oblique or transverse dislodging forces of several different cast gold crowns fabricated to fit stainless steel dies of 5, 10, and 15 degrees of taper, and 4, 6, 8, 10 millimeters in length. Twelve of the test dies are to have parallel axial grooves and twelve are to be without grooves.

TECHNICAL APPROACH

1. To fabricate 12 stainless steel dies of three different tapers and four different lengths. 2. Solid gold castings will be fabricated for these 12 dies. 3. Using an "Instron" testing device, the restorations will be loaded until the castings are dislodged. 4. Using the data from the Instron, the 12 samples will be compared as to relative point of dislodgement. 5. Two parallel grooves will be placed in the axial surface of each die previously tested. 6. Twelve new cast gold restorations will be fabricated for the modified dies. 7. The 12 new castings will be cemented as done previously. 8. Using the Instron testing device, an oblique load will again be placed on each casting, until the castings are dislodged. 9. The data from the last 12 tests and previous 12 tests will be compared and graphic as well as numerical comparisons will be made.

Manpower: None

Funding:	FY 1976
Consumable Supplies	$430.80

C-31-76 (continued)

PROGRESS

1. The superior loading device for the Instron has been fabricated.
2. The inferior loading device for the Instron is being completed.
3. Nine of the first 12 castings have been completed and are ready for testing.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Tissue Response to Metal Versus Acrylic Denture Base Materials.

WORK UNIT NO.: C-36-76

PRINCIPAL INVESTIGATOR: John W. Cressler, D.D., MAJ, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To clinically evaluate the response of supporting tissue in contact with metal as compared to acrylic based dentures in the same oral environment.

TECHNICAL APPROACH

Complete and removable partial dentures will involve the use of acrylic and metal (Ticonium) as the base material. The metal denture base material will be placed in two of four possible quadrants of a complete denture. By doing this in this fashion the acrylic and metal will be randomized in the mouth. Oral tissues will be evaluated at the end of the first, third and sixth month of a six month study.

Manpower: None.

Funding: None.

PROGRESS

This is a new project.

Status: Ongoing

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Microbiologic Comparison of Therapeutic and Disc Antibody Activity Against Selected Enteric Bacteria.

WORK UNIT NO.: C-16-75

PRINCIPAL INVESTIGATOR: Mrs. Cleste N. Guerra, M.S.

ASSOCIATE INVESTIGATORS: Maxine Acosta; Barry Davison, M.S., CPT, MSC; Theodore R. McNitt, M.D., LTC, MC

OBJECTIVES

1. To determine the sensitivity patterns of therapeutic antibodies and antibiotic-impregnated discs.
2. To develop and perform antibiotic sensitivity tests designed to compare the effectiveness of both laboratory methods in relation to proper patient care.
3. To provide better laboratory indices by which physicians may more accurately assess the drug of choice in treatment of patient infections.

TECHNICAL APPROACH

Tube dilution tests of therapeutic and diagnostic (disc) Gentamicin were performed in conjunction with commercially-prepared Gentamicin disc tests against selected patient strains of Serratia sp. Known concentrations of therapeutic Gentamicin were performed in the order of 20, 10, 5.0, 2.5, and .6 mcg/ml. The diagnostic disc 10 mcg (aqueous solutions) were diluted accordingly: 1:2, 1:4, 1:8, 1:16, 1:32, and 1:64.

A series of 21 sensitivity tests have been performed since the last progress report. Each test consisted of organisms recovered from about 30 patients. Fourteen tests were performed by tube dilution methods in comparison with seven tests performed by the Bauer-Kirbey plate sensitivity method. Thus far Klebsiella sp., E. coli, Enterobacter, and Serratia have been tested against Gentamicin and Vibramycin.

Manpower: None.

Funding:	FY 1976	FY 1975
Consumable Supplies	$ 0.00	$0.00
Capital Equipment	$930.00	$0.00

C-16-75 (continued)

PROGRESS

The following is a summary of the preliminary evaluation of current results:

1. Microbiological assays of Gentamicin and Vibramycin sensitivity discs demonstrate a direct correlation with assays of the same therapeutic drugs. All tests show similar results. However, it should be noted that since the disc in tube dilution was already diluted 1:2 then it appears that the evidence suggests:

a. A question of how much actual antibiotic is in each. In other words, are we reporting sensitivity to 10 mcg, 5 mcg or less?

b. The indications are that we report an arbitrary 10 mcg disc sensitivity of an organism which is actually sensitive to 5 mcg or less -- this is one view.

Another view may be noted from the evidence of consistent patterns of these comparison tests which confirm the validity of the experimentally-designed tests of the tube dilution method.

2. Evidence from the therapeutic and diagnostic disc tube dilution tests contradict the disc-plate method, i.e., tube dilution results were considered resistant whereas the disc test results would have been considered sensitive.

In the case of E. coli, for example, it is conceivable that numerous separate source strains would be sensitive to the same drug at the same concentration; it is also reasonable to expect this occurrence to be a mathematical improbability (i.e., millions of organisms would not be expected to react the same way all the time). This is particularly true with multivariable testing methods, such as the disc method. This evidence suggests that all E. coli strains are disc sensitive.

3. The accepted levels of bacterial sensitivity resistance to newer drugs (bactericidal or bacteriostatic) are essentially arbitrary because they are based on experimentally-controlled tests that often do not apply to the clinical laboratory determinations and consequent clinical treatment based on these restuls.

4. In addition, the disc-plate sensitivity does not offer any clue or suggestion as to the actual sensitivity of any given organism. Therefore, disc concentrations based upon achievable serum levels are

C-16-75 (continued)

particularly tenuous because an individual patient's metabolism, with the concomitant infecting organism (infectious process) invariably influences the actual activity of any drug administered. Example factors: drug deterioration, drug concentration, length of treatment, serum concentration, excretion (urinary: Literature indicates - great amounts of any drug are excreted in the six hours post-drug.)

5. The purpose of this study is given further emphasis because pilot test results have confirmed the experimental design, i.e.:

a. Offer more definitive sensitivity results.

b. Provide physicians with laboratory data of practical clinical value.

c. Provide more and newer research data not yet available in the literature.

Status: Ongoing.

Guerra, C.N. and Pindak, F.F. Most suitable substrate selector for differentiation between paired unknown members of enterobacteriaceae. A Clinical and Laboratory Investigation Report. Distributed to all Armed Forces Medical Centers and Hospitals.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Application of the Fluorescent Antibody Technique to the Investigation of Various Dermatoses.

WORK UNIT NO.: C-44-72

PRINCIPAL INVESTIGATOR: Richard L. DeVillez, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To demonstrate the presence or absence of skin auto antibodies or antibodies in the epithelium or sera of patients with a variety of bullous and nonbullous dermatoses.

TECHNICAL APPROACH

Direct and indirect immunofluorescence has been performed on approximately 300 tissue specimens in FY 75.

Manpower: None

Funding:	FY 76	FY 75	FY 74	FY 73
Consumable Supplies	$ 0.00	$0.00	$277.90	$200.00
MEDCASE	$1,734.00	$0.00	$ 0.00	$ 0.00

PROGRESS

The results of the fluorescent work are being evaluated. The service continues to be offered at this hospital and outlying hospitals using the fluorescent fixative.

Status: Ongoing

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Minocin Treatment of Gonorrheal Urethritis.

WORK UNIT NO.: C-129-72

PRINCIPAL INVESTIGATOR: Charles W. Lewis, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To ascertain the best therapeutic dose of Minocin for Treatment of acute gonorrheal urethritis in outpatients.

TECHNICAL APPROACH

Two dosage schedules are utilized with the drug randomized so that the physician does not know what dosage the patient will receive.

Gram stains, cultures, and VD-G Dri-Dot test will be done pre-therapy, at 48 hours and 7 days post-therapy. Blood will be drawn to determine serum levels of Minocin. These samples will be evaluated by Lederle Laboratories.

Manpower: None.

Funding: None.

PROGRESS

This study has been completed. However, the final results have not been received from Lederle Laboratories.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Simultaneous Determination of Instantaneous Aortic Flow, High Fidelity Intracardiac Pressures, Intracardiac Phonocardiography, Echocardiographic Dimensions, and Derived Indices in Man.

WORK UNIT NO.: C-28-73

PRINCIPAL INVESTIGATOR: Joseph P. Murgo, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Stephen A. Altobelli, 1LT, SC; James F. Dorethy, M.D., MAJ, MC; Barry Alter, M.D., MAJ, MC; Harold Felter, M.D., MAJ, MC; John Logsdon, M.D., MAJ, MC; Gwynne Floyd, M.D., MAJ, MC; George C. McGranahan, Jr., M.D., COL, MC; John Paul Giolma, Ph.D., CPT, MSC

OBJECTIVES

1. To develop new techniques in cardiac catheterization, especially in the area of multi-solid state sensor catheters including high fidelity pressure sensors and electromagnetic flow meters. To utilize high speed biplane angiography and external echocardiography in conjunction with such techniques.

2. To utilize these techniques to define sophisticated parameters of ventricular function in patients with various cardiac diseases.

3. To develop specialized computer-assisted analyses of the data derived from such studies.

4. To quantitate left ventricular hydraulic output power.

5. To measure aortic and pulmonary artery input impedance by Fourier analysis and to determine the effect of changing physiologic states upon the impedance.

6. Detailed description of multiple specific objectives are to be found in the original protocol.

TECHNICAL APPROACH

All adult patients for routine right and left heart catheterization are evaluated in the usual manner by a cardiac fellow prior to catheterization. This evaluation includes strip chart echocardiography to

determine the patient's suitability for certain aspects of the protocol. During catheterization, a special, custom-designed, triple-tip, right-heart catheter is introduced into the right heart and simultaneous high fidelity pressures are measured from the pulmonary artery, right ventricle and right atrium. (Significant technical advances since last years report now permit a custom designed and fabricated electromagnetic flow velocity transducer to be located on this same catheter at the site of the pulmonary artery pressure sensor.) A second, more conventional catheter is introduced into the pulmonary artery for purposes of blood specimen withdrawal, thermal dilution cardiac outputs, etc. The left heart is catheterized using a multisensor, custom-designed catheter such that high fidelity left ventricular and aortic pressures are measured as well as ascending aortic electromagnetic flow velocity. During this past year, significant technical advances have been made in this latter configuration. Similar to the right heart catheter, electromagnetic flow velocity is measured at the same location as aortic pressure rather than some distance away as the case was previously. Patients are studied during both rest and supine exercise. In some protocols, depending on the patient's disease, they are studied utilizing a variety of other stresses. Following the collection of hemodynamic data, the patients undergo external echocardiography while pressures and flows are measured simultaneously. The study is terminated after bi-plane ventricular angiography and coronary arteriography if indicated.

Patients undergoing catheterization with the flow catheters also have aortic route angiography and/or pulmonary arteriography for puposes of determining aortic route or main pulmonary artery diameters. These are necessary to calculate flow velocity from volumetric flow itself.

An on-line Honeywell 316 computer presently exists in the laboratory and is capable of sampling all pressures, electrocardiogram, and flows simultaneously. This computer prints out the results of all these parameters immediately, thereby simplifying data analysis immensely.

The specially designed research programming described in last year's progress report has been implemented and considerably enhanced. Temporal relationships between electrical and mechanical events, pressure and flow intervals, hydraulic output power, and systemic and pulmonary input impedance using Fourier analysis have been implemented and tested. As many as 24 consecutive cardiac cycles can be analyzed in a single 8 second sample, with approximately 900 calculated parameters displayed in a matter of seconds.

Angiograms and echocardiograms are analyzed using the Hewlett Packard programmable calculator and digitizer.

C-28-73 (continued)

An extremely sophisticated data retrieval system has been generated using the mass memory purchased in the past year.

Manpower: 1 CPT (6 months)
1 1LT (10 months)
1 SP5 (5 months)
1 SP3 (10 months)

Funding:	FY 76	FY 75	FY 74	FY 73
MEDCASE	$48,902.82	$33,653.44	$29,354.25	$43,000.00
Consumable Supplies		$ 129.76		
Reprints	$ 245.00			
Contractural Svc			$43,573.00	
Capital Equipment			$ 862.40	
TDY		$ 1,018.00	$ 1,195.68	

PROGRESS

Continued progress has been made in the development and implementation of new instrumentation, computer programming, and the application of these techniques to various clinical disorders. In addition to continued measurements of blood flow and derived indices in the ascending aorta, for the first time in man simultaneous measurements of the same parameters have been made in the pulmonary artery in a significant number of patients. Both pulmonary artery and aortic flow velocity are now measured at the identical location of the aortic and pulmonary artery pressure sensors which is a significant improvement over previous techniques. Development efforts are underway to evaluate the possibility of instantaneous aortic and pulmonary artery diameter and flow velocity using ultrasound pulse doppler techniques. The echocardiographic versus angiographic study has continued to expand in the number of patients studied. Hydraulic input power to the systemic circuit has been measured and reported to both the bioengineering and clinical cardiology scientific sessions as indicated below. Systemic input impedance using Fourier analysis of aortic pressure and flow signals have been analyzed in a significant number of normal subjects during both rest and dynamic exercise for the first time. A new cardiac catheterization laboratory using state of the art radiographic and data processing technology is just about completed and will represent a significant advantage in the work for the following year.

Status: Ongoing.

Altobelli, S.A., Murgo, J.P., and McGranahan, G.M. Instantaneous external power development of the left ventricle during rest and exercise in man. Cicrulation, Supp II, 52:592, 1975.

C-28-73 (continued)

Murgo, J.P., Altobelli, S.A., and McGranahan, G.M. A comparison of instantaneous right and left heart ejection dynamics in man. Circulation, Supp II, 52:192, 1975.

Murgo, J.P., Altobelli, S.A., et al. Normal ventricular ejection dynamics in man during rest and exercise. American Heart Association Monograph No. 46, page 92, Sept 1975.

Murgo, J.P. and Altobelli, S.A. Simultaneous left heart echocardiography in multi-sensor catheterization with computer display of pressures, flow, and left ventricular dimensions. Proceedings of 28th Annual conference of Engineering in Medicine and Biology, Vol 17, page 124, Sept 1975.

Murgo, J.P. Multi-sensor cardiac catheterization - new methods to study cardiovascular dynamics in man. Proceedings of 28th Annual Conference of Engineering in Medicine and Biology, Vol 17, page 503, Sept 1975.

Murgo, J.P. New techniques in cardiac catheterization: the advantages of multi-sensor catheters. Proceedings of the 1st International Conference on Biomedical Transducers, Vol II, page 41, Nov 1975.

Murgo, J.P., Giolma, J.P., and Altobelli, S.A. An automated system of processing hemodynamic signals for research in a clinical setting. Digest of the 11th International Conference on Medical and Biological Engineering. (In Press) Ottawa, Oct 1976.

Giolma, J.P. and Murgo, J.P. Signal acquisition and processing for human hemodynamic research. Special Issue on Biological Signal Processing, Proceedings for the IEEE. (In Press) March 1977.

Simultaneous left heart echocardiography and multi-sensor catheterization with computer display of pressures, flow, and left ventricular dimensions. Presented to the 28th Annual Conference of Engineering in Medicine and Biology, New Orleans, La., Sept 1975.

Multi-sensor cardiac catheterization - new methods to study cardiovascular dynamics in man. Presented to the 28th Annual Conference of Engineering in Medicine and Biology, New Orleans, La., Sept 1975.

New techniques in cardiac catheterization: the advantages of multi-sensor catheters. Presented to the 1st International Conference on Biomedical Transducers, Paris, France, Nov 1975.

C-28-73 (continued)

Seminar on cardiovascular pressure and flow dynamics in man. Presented to the Istituto de Ricerche Cardiovascolari at the University of Milan, Milan, Italy, Nov 1975.

A comparison of instantaneous right and left heart ejection dynamics in man. Presented to the 48th Scientific Sessions of the American Heart Association, Anaheim, Calif., Nov 1975.

Instrumentation in Cardiology - 1976. Seminar to the Student Session of the IEEE, University of Texas, Austin, Tex., Apr 1976.

Hemodynamic and flow velocity measurements in atherosclerotic heart disease at rest and during supine exercise. Fifth Meeting of the Association of Army Cardiology, Denver, Colo., May 1976.

Left ventricular function in mitral stenosis: a reassessment. Fifth Meeting of the Association of Army Cardiology, Denver, Colo., May 1976.

The capabilities of a dedicated cardiac catheterization laboratory minicomputer for hemodynamic research. Fifth Meeting of the Association of Army Cardiology, Denver, Colo., May 1976.

Right and left heart ejection dynamics during the Valsalva maneuver. Fifth Meeting of the Association of Army Cardiology, Denver, Colo., May 1976.

Instantaneous left ventricular external power development in congestive cardiomyopathy. Fifth Meeting of the Association of Army Cardiology, Denver, Colo., May 1976.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Calcium Metabolism During Acute Renal Insufficiency.

WORK UNIT NO.: C-40-73

PRINCIPAL INVESTIGATOR: Richard H. Merrill, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: Daniel Nash, M.D., MAJ, MC

OBJECTIVES

To determine the mechanism of hypercalcemia seen in some cases of acute renal insufficiency.

TECHNICAL APPROACH

All patients with acute renal failure will be surveyed. They will be divided into two groups in an alternate manner. The usual dietary and chemotherapeutic modalities for treating acute renal failure will be employed. Hemodialysis and peritoneal dialysis will be reserved for those patients who are uremic or in whom fluid and potassium balance cannot be controlled by conservative means. Serum phosphorus will be maintained below 6 mg% in one group, and the second group will go untreated. For those able to eat, 1000 mg calcium and 1500 mg phosphorus will be offered. Percutaneous renal biopsies will be examined by light microscopy, electron microscopy and immunofluorescent microscopy. Patients with acute renal insufficiency will have three 6-hour dialyses a week. Serial determinations will be done to detect any manifestations of hypercalcemia. In addition, serum parathyroid hormone will be measured and an attempt will be made to correlate the hypercalcemia that is frequently seen following acute renal insufficiency with increased parathormone secretion.

In those patients developing hypercalcemia in the diuretic phase, efforts will be made to suppress parathormone secretion by calcium infusion or phosphorus depletion. When possible weekly eye examination will be performed to document early metastatic calcification. Skin biopsies will be analyzed for calcium.

Manpower: None.

Funding: None.

C-40-73 (continued)

PROGRESS

No patients have been entered into this study. Dr. Ralph Goldsmith, a major collaborator on this project, was to have measured the serum parathormone levels; however, Dr. Goldsmith left his position at the Mayo Clinic and became Chief of Medicine at Audie Murphy VA Hospital in San Antonio, Texas which resulted in a considerable disruption of his laboratory operation. He has not reinstituted the assay for parathyroid hormone and therefore we have been unable to pursue this project. It is anticipated within this coming year that the assay will again be available and this project will be completed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: In vitro Susceptibility of Candida and Torulopsis Species Isolated from Hospitalized Patients to Nystatin, 5-Fluro-cytosine and Amphotericin B.

WORK UNIT NO.: C-2-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To compare in vitro susceptibility of Candida and Torulopsis species isolated from patients who are receiving broad spectrum antibacterial or antifungal agents against similar species isolated from hospitalized patients who are not receiving such agents.

TECHNICAL APPROACH

One hundred and one isolates were tested against Nystatin, Amphotericin B and 5-flurocytosine. Strains isolated from patients were studied. Sensitivity testing was done by tube dilution technique, carried out in duplicate for each isolate.

Manpower: None.

Funding: None.

PROGRESS

One hundred and one strains were tested to Candicidin, a polyene antifungal agent. All of the strains tested were sensitive at 0.195 mcg/ml or less. There was a 16% resistance to 5-flurocytosine; however, all organisms were sensitive to both Amphotericin B and Nystatin. When the degree of sensitivity with the three polyene antifungal agents Amphotericin B, Nystatin and Candicidin were compared, there was a suggestion of dissimilarity with certain strains being sensitive to one agent at

C-2-74 (continued)

very high MIC's and to one of the other agents at very low MIC's. This suggests the potential of stepwise resistance.

Status: Completed.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Physiologic Evaluation of Pulmonary Status in Patients Undergoing Renal Dialysis.

WORK UNIT NO.: C-4-74

PRINCIPAL INVESTIGATOR: William W. Burgin, Jr., M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the pulmonary function in renal dialysis patients both pre- and post dialysis and to better ascertain the physiologic changes which take place in the lung.

TECHNICAL APPROACH

Complete pulmonary function tests pre- and post dialysis to include oxygen dissociation curve shifts, cardiac outputs, oxygen uptakes, pulmonary compliance, and spirometric measurements are performed.

Manpower: None.

Funding: None.

PROGRESS

Generally, the studies are as predicted in that the patients who undergo pulmonary function evaluation before dialysis tend to do more poorly than those same patients after undergoing dialysis. Progress has been slow.

Status: Ongoing.

C-4-74 (continued)

State of the art of pulmonary physiotherapy. Presented to the Texas Medical Association, 7 May 1976, Dallas, Texas.

Drugs producing abnormal chest findings. Presented to the U.S. Army Pulmonary Symposium, Fitzsimons Army Medical Center, September 1975, Denver, Colorado.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II Study of Aminoglycoside Antibiotic BB-K8.

WORK UNIT NO.: C-8-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To evaluate therapeutic effectiveness of BB-K8 in the treatment of hospitalized patients with infections caused by susceptible pathogens.
2. To establish an optimal therapeutic dosage schedule for BB-K8 which is safe and effective.
3. To establish a side effect profile for the drug.
4. To obtain information on the clinical pharmacology of the drug in diseased patients.

TECHNICAL APPROACH

BB-K8 is given by deep intramuscular injection at the appropriate site at a dose not to exceed 7.5 mg/kg every 12 hours. Each patient and his clinical record will be evaluated twice a day throughout the course of drug therapy. Patients with urinary infections will have repeat urine culture and colony counts at 48 to 72 hours after initiation of therapy. Each patient will be followed by daily urinalysis with microscopic examination. BUN and creatinine determinations will be performed every 48 hours throughout the period of drug administration. Audiograms will be performed on the 3rd, 6th and 10th days of therapy. Appropriate specimens will be forwarded to Bristol Laboratories for determination of BB-K8 concentrations. Appropriate post treatment cultures will be obtained at the conclusion of BB-K8 therapy. Repeat chest x-rays will be obtained and patients with septicemia will have post treatment blood cultures.

Manpower: SP5 (2 months)

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$ 0.00	$82.74	$51.30

C-8-74 (continued)

PROGRESS

Since the last report this antibiotic has been placed in a Phase III category. An additional patient has been treated with a good clinical and bacteriological response. The current plan is to establish a homogeneous patient population which by virtue of underlying disease will require this type of antimicrobic chemotherapy. The thermally injured patient is one such group. A proposal has been submitted to the Institute of Surgical Research, Brooke Army Medical Center, for use of BB-K8 in patients with resistant gram negative bacterial infections. Further evaluation of this antibiotic is planned.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Class II Clinical Study of Ticarcillin (BRL 228).

WORK UNIT NO.: C-10-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the effectiveness and safety of various dosages of Ticarcillin in the treatment of infections in hospitalized patients where those infections are the result of susceptible organisms: E. coli, Proteus mirabilis, Proteus morganii Proteus rettgeri, Proteus vulgaris, Providencia stuartii, Pseudomonas aeruginosa, Mima, Herellea, Enterobacter aerogenes, Enterobacter cloacae, Citobacter freundii, and Serratia marcescens.

TECHNICAL APPROACH

Patients with infections secondary to sensitive gram negative rods, after receiving informed consent, were treated with intravenous Ticarcillin at a dose of 300 mg/kg/24 hours. CBC, platelet and bleeding time, SMA-18, urinalysis and susceptibility testing were performed when indicated. All examinations were performed prior to starting therapy, during therapy and 24 hours following cessation of therapy. Antibiotic levels were obtained. Using a random number table, patients were randomized either to a Ticarcillin category or a Carbenicillin category.

Manpower: SP5 (2 months)

Funding:	FY 76	FY 75
Consumable Supplies	$405.60	$262.86

PROGRESS

Eight patients were treated in a randomized fashion, four received Carbenicillin and four received Ticarcillin. During this phase of testing, phlebitis developed in three of the four patients treated

C-10-74 (continued)

with Ticarcillin and a skin rash developed in the fourth. Because of the high incidence of thrombophlebitis associated with the intravenous administration of this drug, further use was discontinued.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Transfusion - Efficiency and Methods to Improve Current Results in Thrombocytopenia Patients.

WORK UNIT NO.: C-16-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To improve the quality of platelet transfusions in thrombocytopenic patients and platelet transfusion complications.

TECHNICAL APPROACH

The use of several methods of identifying platelet antibodies, i.e., serotonin release, complement fixation and platelet aggregation methods, are being evaluated to determine the presence of platelet antibodies in both the transfused patients and to identify a select group of potential donors who have platelets compatible with the recipient. Techniques of antibody identification are being evaluated as well as the effectiveness of platelet therapy with this method of cross-matching.

Manpower: SP4 (2 months)

Funding:	FY 76	FY 75
Consumable Supplies	$301.10	$345.15

PROGRESS

Marked progress in technical methodology of the serotonin release assay has been made in the past twelve months. The procedure has been shortened from four hours to approximately one hour and twenty minutes for running a set of samples to include as many as 60 samples. Currently random volunteer donors' platelets are being stored for cross-matching against a potential recipient serum to identify those donors who would have compatible platelets for transfusion into thrombocytopenic patients

C-16-74 (continued)

with the presence of platelet antibodies. Preparation of a manuscript presenting technical aspects of the revised serotonin release assay is being prepared. Preparation for submission of platelet antibody identification data and platelet cross-matching data to The American Society of Hematology meeting in December 1976 is being prepared.

Status: Ongoing.

Utilizing the Cell Harvester and Preserved Labelled Platelets to Simplify the [^{3}H] Serotonin Release Assay for the Detection of Platelet Isoantibodies. Master's thesis by Daniel J. Marmer presented in February 1976 through Division of Graduate Studies at Incarnate Word College, San Antonio, Texas.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Correlation of Specific and Total IgE Globulin Levels in the Serum to Specific Skin Tests.

WORK UNIT NO.: C-18-74

PRINCIPAL INVESTIGATOR: Bryan R. Updegraff, M.D., MAJ, MC

ASSOCIATE INVESTIGATOR: Hobert L. Pence, M.D., MAJ, MC

OBJECTIVES

To correlate the levels of specific circulating antibodies in the serum with intracutaneous skin tests in mountain cedar sensitive patients.

TECHNICAL APPROACH

Prior to the Mountain Cedar pollen season, 40 patients were selected. The treatment group received aqueous extract of Mountain Cedar pollen subcutaneously as tolerated to a maintenance dose of 0.3 cc of a 1:50 w/v concentration. The second group, or placebo group, received injections of caramalized glucose with histamine added to simulate the appearance and local reactions caused by the true extract. The patients were placed on the same injection schedule which started injections at a thousand fold dilution of the full strength concentration. Specific anti-Mountain Cedar IgE antibody levels in the sera of the patients were measured by means of the radioallergosorbant test (RAST). Evaluation of the patients' clinical course throughout the season was performed by having them record symptoms on a daily basis. Thirty-two patients completed the study with 17 in the treated group and 15 in the placebo group.

Manpower: SP6 (2 months)

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$750.00	$1,230.00	$999.00

C-18-74 (continued)

PROGRESS

Specific high dose allergy injection therapy with aqueous extract has been shown to suppress symptoms of respiratory allergy due to pollen from the conifer, Mountain Cedar. This study would seem to add this allergen to the expanding group of inhalant allergens for which controlled studies have demonstrated effectiveness of immunotherapy in suppressing symptoms of respiratory allergy. The injection therapy was accompanied by a drop in specific IgE anti-Mountain Cedar antibodies during the pollen season while untreated patients had an increase in specific IgE levels. This study suggests that immunotherapy can be a helpful addition in treating those patients with Mountain Cedar pollinosis whose symptoms cannot be controlled with pollen avoidance and symptomatic therapy.

Status: Completed.

Pence, H.L., Mitchell, D.Q., Greely, R.L., Updegraff, B.R. and Selfridge, H.A.: Clinical response to immunotherapy for mountain cedar pollinosis: a double-blind controlled study. J. Allerg. Immunol. (In Print).

DEPARTMENT OF THE ARMY
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Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Hypertension with Polycystic Kidney Disease.

WORK UNIT NO.: C-20-74

PRINCIPAL INVESTIGATOR: Daniel A. Nash, Jr., M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the volume status and renin-angiotensin system in patients with polycystic kidneys and unexplained hypertension to clarify the mechanism(s) of the hypertension frequently present in patients with polycystic kidneys.

TECHNICAL APPROACH

Eight polycystic kidney disease patients with hypertension and maintained glomerular filtration rate were studied on known sodium intakes. The renin-angiotensin-aldosterone system, plasma volume, and blood pressure changes were evaluated in relation to sodium intake. In this manner, the contributions of these various factors to the patient's hypertension could be considered.

Manpower: None.

Funding: None.

PROGRESS

The results of this study have been evaluated in six patients. Four PVD-PRA (plasma volume determination-plasma renin activity) patterns were defined. Hypertension was most severe in the four patients with increased PVD, and high or normal PRA. A blunted renin response to volume contraction was seen in three of these four. Blood pressure was significantly improved by volume contraction even in the two with normal PVD. Aldosterone excretion varied directly with renin activity.

C-20-74 (continued)

Volume expansion due to sodium retention appears to contribute to hypertension in all six polycystic kidney disease patients. However, severe depression of PRA was never seen, and three patients had increased baseline PRA. Three patients with renal vein renin assays had significant differences between renin production from the right and left kidneys. Two of these fulfilled criteria for unilateral ischemia. It appears that vascular distortion due to severe cystic disease results not only in consistent Na retention, but also in variable stimulation of renin.

Status: Completed.

Nash, D.A., Jr. Etiology of hypertension in polycystic kidney disease patients with maintained GFR. Kidney International, Vol. 8, No. 6, page 442, Dec. 1975; cited in news release - Hypertension, Vol. 2, No. 3, Mar 1976.

Etiology of hypertension in polycystic kidney disease patients with maintained GFR. Presented to the American Society of Nephrology, Nov 1975.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Radioactive Serotonin Release Assay and Lymphocyte Thymidine Uptake as a Means of Platelet Antibody Identification.

WORK UNIT NO.: C-22-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the relative specificities of these assays and to evaluate their clinical usefulness.

TECHNICAL APPROACH

Comparison of radioactive serotonin assay as described in previous protocols and lymphocyte thymidine uptake as a means of platelet antibody identification have been made on several occasions.

Manpower: None.

Funding: None.

PROGRESS

To date, the ability of the serotonin release assay to identify platelet antibodies has proved exceptional. At present, lymphocyte thymidine uptake as a means of platelet antibody identification has proved to be a tedious, time consuming procedure with very poor results in identifying antibodies other than very markedly positive isoantibodies. The usefulness of this procedure has been supplanted by other procedures.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Function in the Presence of Varied Platelet Antibodies.

WORK UNIT NO.: C-23-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the capability of platelet function when stressed by a variety of platelet antibodies.

TECHNICAL APPROACH

Platelet function is measured by clot retraction. Platelet factor III release and platelet aggregation studies are being performed in the presence of platelet antibodies. These antibodies are of the autoimmune, isoantibody and drug induced nature. They are evaluated by the serotonin release assay, complement fixation, platelet aggregation, clot retraction, and platelet factor III release methods.

Manpower: SP4 (6 months)

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$0.00	$0.00	$196.00
Capital Equipment	$0.00	$0.00	$420.00

PROGRESS

To date a number of various antibodies have been examined. In agreement with current literature, it is found that autoantibodies of the ITP nature are extremely difficult to measure or identify and by the present methods have not been identifiable. Platelet isoantibodies are readily identified by the serotonin release assay and in certain cases have been identified by the platelet aggregation method and by the complement fixation method. The serotonin release seems to be

C-23-74 (continued)

more specific; however, further studies are necessary. Two patients with blood induced thrombocytopenia have been evaluated and the antibody has been identified by the complement fixation method and the platelet aggregation method. Modifications of the serotonin release assay method to make the procedure of use in drug induced platelet antibodies are being investigated.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Platelet Factor Four to Evaluate Hypercoagulable States.

WORK UNIT NO.: C-24-74

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To look at the plasma of patients who have a possible setting of hypercoagulability and to evaluate their plasma for platelet factor four activity.

TECHNICAL APPROACH

The release of platelet factor four by platelets in a hypercoagulable state has been reported by some authors to be a means of identifying hypercoagulability. In certain selected cases the study is being performed to evaluate its effectiveness.

Manpower: None.

Funding: None.

PROGRESS

Several patients have been studied; however, to date a direct correlation with the clinical condition has not been established. It is planned to evaluate this procedure in conjunction with oncologic platelets with chronic disseminated intravascular coagulopathy over the next year.

Status: Ongoing.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Ophthalmologic Manifestation of Candida Infection and Hypersensitivity to Candida in Rabbits.

WORK UNIT NO.: C-26-74

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the natural history of candida infection in the eye.

TECHNICAL APPROACH

Twenty New Zealand white rabbits were utilized for the study. The grouping of the rabbits and experimental procedures were outlined in the original protocol. At the time all animals were sacrificed the eyes were submitted for quantitative culture which determined the number of organisms per gram of tissue obtained from one of the two eyes. The second eye was submitted for histologic examination with specific biopsies of the retina and uvea.

Manpower: None.

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$0.00	$0.00	$106.25

PROGRESS

The original results of this study were reported in the Annual Report Fiscal Year 1974. The study has been discontinued because of intrinsic difficulties with quantitation of infection and non-uniform development of ophthalmitis.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Antacid Therapy on Recurrences of Duodenal Ulcer.

WORK UNIT NO.: C-32-74

PRINCIPAL INVESTIGATOR: Richard W. Welch, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Armand Littman, M.D.

OBJECTIVES

To determine whether antacid treatment in duodenal ulcer patients during asymptomatic periods prevents recurrences of complications.

TECHNICAL APPROACH

Double blind prospective trial of antacid vs. placebo to assess recurrence rate in duodenal ulcer progress.

Manpower: None.

Funding: None.

PROGRESS

Terminated due to REFRAD of principal investigator.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phytohemagglutinin Stimulation of Sarcoid Lymphocytes.

WORK UNIT NO.: C-36-74

PRINCIPAL INVESTIGATOR: Hobert L. Pence, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: William W. Burgin, M.D., COL, MC
Robert L. Greely, M.D., COL, MC

OBJECTIVES

To study phytohemagglutinin (PHA) stimulation of lymphocytes from patients with sarcoid and to investigate possible suppression of lymphocyte response by plasma from sarcoid patients.

TECHNICAL APPROACH

This involves studying blastogenesis of the lymphocytes of patients with sarcoidosis in presence of autologous or homologous AB+ blood.

Manpower: None.

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$0.00	$1,418.82	$2,068.50
Capital Equipment			$ 475.00

PROGRESS

Seven patients with sarcoidosis were studied. The plasma of six of the patients caused significant suppression of lymphocyte response to PHA. This project is terminated due to lack of adequate number of patients and departure of principal investigator.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Evaluation and Treatment of Male Infertility.

WORK UNIT NO.: C-39-74

PRINCIPAL INVESTIGATOR: K. James Ehlen, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., COL, MC
Mauro P. Gangai, M.D., COL, MC

OBJECTIVES

To rule out any surgically or medically correctable causes of male infertility and to treat the idiopathic oligospermic or asthenospermic infertile patient with human gonadotropin (human chorionic gonadotropin).

TECHNICAL APPROACH

The male partners of infertile couples will be evaluated initially with a semen analysis. If this is abnormal in any way then they will be evaluated by an endocrinologist. If no specific endocrine syndrome is found, the patient will then be referred to Urology for a biopsy of the testes. This is done to differentiate the patient who has normal seminiferous tubule function with blockade of the exit tubes from those who have primary seminiferous tubule hypofunction. The patients who have no blockade of the tubes will then be given the opportunity to participate in this program which consists of injecting them with human chorionic gonadotropin once a week for a minimum of six months with periodic physical examinations and assays for testosterone and semen analysis. Patients who have a specific endocrine syndrome or a urological defect will receive th, therapy indicated and will not be entered into the study.

Manpower: None.

Funding: None.

PROGRESS

In the last 12 months no new patients have been entered into this study. The study is terminated due to lack of adequate patient material.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Antigens in Fire Ant Venom.

WORK UNIT NO.: C-41-74

PRINCIPAL INVESTIGATOR: Frank K. James, Jr., M.D., COL, MC

ASSOCIATE INVESTIGATORS: Hobert L. Pence, M.D., MAJ, MC
Donald P.Driggers, CPT, MSC

OBJECTIVES

To study the venom and/or its component parts and its effect on selective human volunteers known to be sensitive to the fire ant venom.

TECHNICAL APPROACH

Venom was gathered from the two imported species of ants and prepared for use in specific skin testing on fire ant sensitive patients and controls. Twenty-five fire ant sensitive patients and 15 control patients were studied in detail.

Manpower: None.

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$0.00	$ 75.96	$115.00
TDY			$366.00

PROGRESS

Venom, as well as whole body extract (WBE), of the imported fire ant appears to be a useful tool in evaluating hypersensitivity by skin testing and may, in fact, be a more sensitive indicator whan WBC. Available evidence suggests cross-reactivity or shared antigens between fire ant venom, WBC, and WBC of other Hymenoptera species. This is true even though the venoms of fire ants and other Hymenoptera are vastly different. Passive transfer studies suggest the positive skin tests are mediated by an IgE mechanism. Fire ant

C-41-74 (continued)

hypersensitivity may be a useful model for future studies of mechanisms and treatment of Hymenoptera hypersensitivity, since fire ant venom is relatively simple when compared to venoms of other species and active components of the venom can be synthesized. In vitro immunologic studies are needed to better define the components of the venom responsive for hypersensitivity.

Status: Ongoing.

James, F.K., Jr., Pence, H.L., Driggers, D.P., Jacobs, R.L. and Horton, D.E. Fire ant hypersensitivity. Studies of human reactions to fire ant venom. J. Allerg. Clin. Immunol. (In Press).

In vivo and in vitro studies of fire ant venom. Presented to American Academy of Allergy, San Juan, Puerto Rico, 6-10 Mar 1976; Annual Imported Fire Ant Research Conference, Gulfport, Miss., 29-31 Mar 1976; Southwest Allergy Forum, 22-25 May 1976.

DEPARTMENT OF THE ARMY
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CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Rejection of Verrucae Vulgaris - A Clinical Therapeutic Trial. Parts I and II. (Collaborative Study with Letterman)

WORK UNIT NO.: C-6-75

PRINCIPAL INVESTIGATOR: Joseph H. Greenberg, M.D., MAJ, MC (LAMC)

ASSOCIATE INVESTIGATORS: Charles W. Lewis, M.D., LTC, MC
Nikolajs Lapins, M.D., MAJ, MC

OBJECTIVES

To determine if induction of a delayed hypersensitivity reaction over a verruca vulgaris will cause destruction of the verruca and possibly cause regression of other verrucae vulgaris not treated.

TECHNICAL APPROACH

Patients with verrucae vulgaris agreeing to participate in the study have their warts treated either with topical Rhus oleoresin (if they have a positive history of Rhus dermatitis) or they receive an intradermal injection of one of the common skin test antigens into a wart. This group of patients is screened by testing with Mumps, Candida, PPD, SK-SD and Trichophyton, and the antigen giving the strongest reaction is selected for testing.

Manpower: None.

Funding: None.

PROGRESS

Fifty-four patients have completed the study. The intradermal antigen group of 34 patients has shown successful therapeutic results with only Trichophyton. The other antigens have been discontinued. The Rhus study group of 17 patients has resulted in approximately 50% successful results. It is anticipated that the protocol may be modified to a multiple application of the antigen to determine if this mode of therapy will be successful in improving the cure rate.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Incidence of Transient Bacteremia during Bronchoscopy.

WORK UNIT NO.: C-8-75

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: William W. Burgin, Jr., M.D., COL, MC
Robert B. Blumer, M.D., LTC, MC

OBJECTIVES

To determine the incidence of bacteremia as a result of bronchoscopy using the fiberoptic bronchoscope in patients undergoing diagnostic bronchoscopy.

TECHNICAL APPROACH

Patients undergoing diagnostic bronchoscopy after having given informed consent had throat cultures performed. Following throat cultures, a blood culture was obtained at time zero. Bronchoscopy was then performed and at 5, 15 and 30 minutes following bronchoscopy, blood cultures were obtained for aerobic and anaerobic specimens. Bronchial washings were cultured during the bronchoscopy and these culture results compared.

Manpower: None.

Funding:	FY 76	FY 75
MEDCASE		$4,705.00

PROGRESS

Eleven patients had single positive blood cultures; the organisms isolated included Staph epidermidis (4), propionibacterium acnes (5), serratia marcescens (1), and corynebacterium sp. (1). Three additional patients had blood cultures positive for Staphylococcus epidermidis. Throat cultures were unrewarding. Bronchial washings were positive in 19 and negative in 5 patients. In only two patients the organisms obtained by blood culture matched those species obtained

C-8-75 (continued)

by bronchial washings; both of these organisms were Staphylococcus epidermidis. No correlation existed between length of procedure, whether or not brushing and/or biopsy was performed, and positive blood cultures. Sepsis did not occur clinically in any patient post-bronchoscopy, as evidenced by absence of fever or hypotension.

This study supports recently published data concerning the absence of significant bacteremia during bronchoscopy.

Status: Completed.

Incidence of Transient Bacteremia During Bronchoscopy. Presented to American College of Chest Physicians.

Brearley, C.B. Incidence of transient bacteremia during bronchoscopy. Submitted for publication.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Outpatient Algorithm Validation - A Pilot Study.

WORK UNIT NO.: C-9-75

PRINCIPAL INVESTIGATOR: Barry W. Wolcott, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Leslie M. Burger, M.D., LTC, MC
Richard K. Tompkins, M.D., Dartmouth Medical School

OBJECTIVES

To determine if clinical outpatient algorithms originally used to treat civilian outpatient populations can be validated and improved in a military outpatient environment - a Phase I study.

TECHNICAL APPROACH

Patients evaluated by physician extenders (AMOSIST's) for certain specified complaints are contacted at specified follow-up intervals by specially trained research assistants who obtain specific outcome data. Additionally, randomly selected patients are independently re-evaluated by board certified internists and discharged on the treatment prescribed by the internists. The internists are unaware of the evaluation or therapy performed by the physician extenders. Patients seen by the board certified internists are also studied by the research assistans at fixed follow-up intervals. In this way, retrospective analysis of prospectively collected patient data can be performed and comparisons made in the process and outcome of AMOSIST's compared to that of board certified internist's.

Manpower: None.

Funding:	FY 76	FY 75
Consumable Supplies	$0.00	$3,125.00
TDY	$0.00	$ 75.00

PROGRESS

To date we have studied approximately 4,000 patients seen and treated in the AMIC and an additional 500 seen and treated by the control

C-9-75 (continued)

internist's. For patients with complaints suggesting acute respiratory illness (21% of all walk-in patients treated at the AMIC) AMOSIST-directed care shows outcome identical to that of board certified internists with significantly lower costs for AMOSIST evaluation. The performance of the BAMC AMOSIST's has been compared to that of civilian physician extenders using the same clinical algorithms and no statistically significant difference in these two provider groups has been noted.

Status: Ongoing.

Data presented at the Federation for Clinical Investigation meeting, Atlantic City, 2 May 1976, and at the University Association of Emergency Medical Services meeting, Philadelphia, 12 May 1976.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Efficacy of Topical Haloprogin in the Treatment of Chronic Tinea Pedis. Phase II Study.

WORK UNIT NO.: C-13-75

PRINCIPAL INVESTIGATOR: Richard L. DeVillez, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: Frank L. Foreman, M.D., MAJ, MC

OBJECTIVES

To determine if 5% haloprogin cream is useful in the treatment of tinea pedis.

TECHNICAL APPROACH

A double blind study comparing the efficacy of topical haloprogin cream 1% vs. 5% for the treatment of chronic tinea pedis.

Manpower: None.

Funding: None.

PROGRESS

Thirty patients were treated using coded tubes of haloprogin cream. No side effects were noted, and the chronically infected feet responded equally well with either concentration of drug used. This correlated well with similar studies conducted at other medical centers.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Function in Patients Undergoing Therapy with Velban and Bleomycin.

WORK UNIT NO.: C-17-75

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate patients undergoing intensive chemotherapy with Velban and Bleomycin for determination of platelet function abnormalities induced by these agents.

TECHNICAL APPROACH

Standard platelet function studies are performed on patients being treated entirely with Velban dn Bleomycin.

Manpower: SP4 (2 months)

Funding: None.

PROGRESS

Patient studies show no significant platelet function abnormality in relation to either one of these drugs, but more patients must be enlisted.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Platelet Function in Patients Undergoing Vincristine Therapy.

WORK UNIT NO.: C-18-75

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine any abnormalities of platelet function occurring in patients who are treated with Vincristine therapy.

TECHNICAL APPROACH

Standard platelet function studies are being performed on patients undergoing Vincristine therapy. It is known that Vincristine increases platelet production and is useful as an agent in non-responsive idiopathic thrombocytopenic patients.

Manpower: None.

Funding: None.

PROGRESS

To date a small number of patients have been studied, receiving Vincristine as a single agent therapy. No functional platelet abnormality has been identified.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Renal Handling of Bicarbonate in Patients with Hyperparathyroidism.

WORK UNIT NO.: C-22-75

PRINCIPAL INVESTIGATOR: David B. Olin, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the effect of parathyroid hormone on bicarbonate absorption in the human model.

TECHNICAL APPROACH

This study was designed to test the patients both pre- and post-operatively after neck exploration for parathyroid adenoma. The intent was to study patients with bicarbonate loading and thus to establish a curve for the relationship between urinary handling of bicarbonate and serum bicarbonate levels.

Manpower: None.

Funding: None.

PROGRESS

No patients have been entered into the study. This project is terminated due to transfer of principal investigator.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Incidence and Characterization of Adrenal Insufficiency in Oat Cell Carcinoma.

WORK UNIT NO.: C-25-75

PRINCIPAL INVESTIGATOR: K. James Ehlen, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Roger L. Wallace, M.D., CPT, MC;
Steven Humphrey, M.D., CPT, MC

OBJECTIVES

To establish the incidence and character of adrenal insufficiency in patients with oat cell carcinoma.

TECHNICAL APPROACH

Patients with a proven diagnosis of oat cell carcinoma are studied with Cortisol response to ACTH infusions and 11-Deoxycortisol and ACTH response to Metapyrone administration.

Manpower: None.

Funding:	FY 76	FY 75
Consumable Supplies	$1,212.00	$1,292.00

PROGRESS

Twenty-one patients with oat cell carcinoma have been studied in a prospective fashion. Evidence for adrenal insufficiency or dysfunction has been found in none of these patients.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Basal Blood Pressures and Casual Blood Pressure Effecting the Therapy of Hypertension.

WORK UNIT NO.: C-26-75

PRINCIPAL INVESTIGATOR: Richard H. Merrill, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if basal blood pressure taken three times daily by the patient or another trained person is significantly different from the casual blood pressure taken during clinic visits.

TECHNICAL APPROACH

Approximately 20 patients were enlisted into this study after obtaining informed consent. Patients were given equipment to take their own blood pressure at home and were asked to take blood pressures three times daily over a four week period. These blood pressures are referred to as home blood pressures and were compared to blood pressures obtained once a week for four weeks in a clinic setting. The clinic blood pressures are referred to as casual blood pressures and were obtained by either a physician on the study or a nurse clinician. The patient's ability to take accurate blood pressures was checked weekly by a nurse clinician. The mean blood pressures obtained at home were compared to the mean casual blood pressures in this group. The data was also evaluated as to whether other treatment choices would have been made if the physician had been aware of the home blood pressures rather than only the weekly casual blood pressures. Systolic blood pressures in excess of 150 or diastolic blood pressures in excess of 90 were considered abnormal and felt to require treatment changes. The casual and home blood pressures were compared and determination was made to see whether the patient was either undertreated or overtreated. In the former situation, he would require additional medication if home blood pressures were known to the physician and were used for treatment rather than his casual blood pressures. In the latter situation, he would require less medication if his home blood pressures were used as a guideline for treatment rather than his casual blood pressures.

Manpower: None.

Funding: None.

C-26-75 (continued)

PROGRESS

Data were collected and evaluated, and it was found that mean blood pressures obtained at home were statistically different than blood pressures obtained casually in the clinic. As a rule, blood pressures tended to be lower at home as compared to casual blood pressures, but this did not hold true for the whole population. Using the treatment guidelines given in the technical approach, the treatment choices comparing casual and home blood pressures did not agree 35% of the time. That is, if home blood pressures were considered to best reflect the patient's hypertensive status then casual blood pressures indicated treatment choices which were wrong 35% of the time.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: In vitro Lymphocyte Stimulation and Leukocyte Inhibitory Factor Assay in Patients Who Have Been Immunized Against Rabies.

WORK UNIT NO.: C-27-75

PRINCIPAL INVESTIGATOR: Adolf E. Rahm, Jr., M.D., LTC, MC

ASSOCIATE INVESTIGATORS: SP6 Hartley A.Selfridge

OBJECTIVES

To study in vitro lymphocyte stimulation and leukocyte migration inhibition in patients who have been immunized against rabies.

TECHNICAL APPROACH

Human lymphocytes are separated from blood specimens by hypaque ficoll gradient. Following several washes they are incubated with rabies vaccine, treated with thymidine, and the rate of lymphocyte stimulation is estimated by the amount of radioactive thymidine taken up. In addition, lymphocytes and leukocytes are cultured in agarose wells with vaccine present to determine the amount of leukocyte migration inhibition.

Manpower: SP6 . (4 months)

Funding: None.

PROGRESS

A number of positive and negative controls have been studied, and it appears that there is nonspecific antigen antibody stimulation of the lymphocytes. This has been determined by incubating cells from non-immunized subjects in wells containing human rabies immune globulin and rabies vaccine.

Status: Ongoing.

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DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Measurement of Transepidermal Water Loss in Anhidrotic Ectodermal Dysplasia and Erythroderma.

WORK UNIT NO.: C-29-75

PRINCIPAL INVESTIGATOR: Robert L. Rietschel, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To measure total body evaporative water loss in skin conditions of excessive and insufficient transepidermal water loss and compare these values with measurements of water loss from small areas of skin.

2. To study the effect of various topical compounds in common dermatologic use on transepidermal water loss in individuals with excess or insufficient water loss.

TECHNICAL APPROACH

An electrolytic moisture analyzer is being utilized to detect evaporative water loss from skin of individuals with excessive and insufficient moisture losses. Total body moisture losses are measured by weight loss in an environmental chamber on a metabolic bed scale.

Manpower: None.

Funding:	FY 76	FY 75
Consumable Supplies		$ 255.95
Rental	$21.00	
MEDCASE		$1,250.00

PROGRESS

Two patients with anhidrotic ectodermal dysplasia were studied and found to be dissipating heat via radiation and conduction/convection at a near normal rate at rest under normal room temperature. With heat stress the radiational and conductive/convective heat losses were insufficient to prevent a rise in core temperature. Evaporative water loss remained near zero.

C-29-75 (continued)

One patient with excessive moisture water loss from his hands due to symmetrical lividity of the palms was studied on various modes of therapy. His evaporative water loss was suppressed by topical aluminum chloride, but the dermatitis persisted. Treatment with Vitamin A acid improved both the dermatitis and the excessive moisture loss. The moisture loss appears unrelated to the skin temperature in this condition..

Status: Ongoing.

Rietschel, R.L, Lewis, C.W., Simmons, R.A., and Phylicky, R.L.: Skin lesions in paroxysmal nocturnal hemoglobinuria. Arch. Derm. (In Press).

Rietschel, R.L. : The effects of prolonged water exposure on human skin: A reassessment. J. Invest. Derm. (In Press).

Rietschel, R.L.: Invisible dermatoses. Cutis (In Press).

Presented to American Academy of Dermatology, 8 December 1975, San Francisco, California.

Presented at the American Medical Association meeting, 29 June 1976, Dallas, Texas.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Role of Prostaglandins (PG) in the Response to Volume Expansion in the Dog.

WORK UNIT NO.: C-30-75

PRINCIPAL INVESTIGATOR: David B. Olin, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Richard H. Merrill, M.D., LTC, MC

OBJECTIVES

To evaluate in the dog model volume expansion, the role of prostaglandins and to determine if the prostaglandins play a role in renal autoregulation.

TECHNICAL APPROACH

This study has been carried out under the auspices of the Institute of Surgical Research and under the direction and assistance of Dr. Richard Merrill, Chief of the Internal Medicine Branch at USAISR. Mongrel dogs receiving volume expansion with either Ringer's lactate or hyperoncotic albumin have had the differences in response to the manipulations on the prostaglandin system utilizing Indomethacin and Meclofenamate as specific inhibitors of prostaglandin synthetase activity. All animals are anesthetized at the time the study is carried out.

Manpower: None.

Funding: None.

PROGRESS

Fifteen dogs have been studied. Investigation has revealed that there is no effect of prostaglandin inhibition on the response to volume expansion with Ringer's lactate, and investigation involving the role of prostaglandin inhibition in response to hyperoncotic volume expansion is currently being investigated. There seems to be no effect of prostaglandin inhibition on the response to hyperoncotic albumin expansion.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Are Prostaglandins Important in the Development of Acute Renal Failure?

WORK UNIT NO.: C-31-75

PRINCIPAL INVESTIGATOR: David B. Olin, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To investigate possible pathophysiologic mechanisms in gentamicin acute renal failure.

TECHNICAL APPROACH

This project was designed in two phases, the first to investigate the possibility of establishing a reliable model of gentamicin nephrotoxic renal failure in rabbits. The subsequent phase was to evaluate the pathophysiologic role of prostaglandin in the development of nephrotoxic nephritis.

Rabbits were selected and divided into groups of two rabbits each receiving varying dosages of gentamicin in an intramuscular injection daily for two weeks. The dose schedule was 10 mg/kilo, 20 mg/kilo, and 40 mg/kilo in the initial phase of the study. The initial six rabbits were treated with daily injections of gentamicin furnished by the Schering Drug Corporation. Following the two weeks of injection, repeat blood studies were evaluated, the animals were sacrificed, and the kidneys were examined by light microscopy. An additional study group compared rabbits placed on varying diets including salt restriction, salt loading and acid loading diets. Two rabbits were placed in each study group and all received a similar dosage of 40 mg/kilo of gentamicin for two weeks. Laboratory data were obtained following renal function and serum electrolytes and at the end of the two week study, the rabbits were sacrificed and tissue was submitted for light microscopy.

Manpower: None.

Funding: None.

C-31-75 (Continued)

PROGRESS

The early phase of this study has revealed that at the dosage tested, and the animals utilized, there was no effect on renal function or on renal pathology after two weeks of high dose gentamicin. In addition, when diets were altered by either acid loading or salt loading, there was also no effect on apparent development of renal insufficiency in these animals.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Simple Biochemical Test for the Screening of Malignancies.

WORK UNIT NO.: C-33-75

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: Harris D. Plant, SP4

OBJECTIVES

To examine the reaction of Ehrlich's reagent with human plasma and to determine if the intensity of the reaction can be correlated with the health of that individual.

TECHNICAL APPROACH

Biochemical test for screening malignancies was investigated.

Manpower: SP4 (6 months)

Funding: None.

PROGRESS

Neuraminic acids which react with Ehrlich's aldehyde reagent and more specific reagents to identify the presence of neoplasms have been reported in the literature. Currently more specific studies for identifying neuraminic acids have been reported and it was found that elevations of these compounds are present in patients with malignancies. Whether these compounds are elevated in other diseases is yet to be determined and is being performed by other laboratories capable of performing the precise studies.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Bone Scanning as a Method for Detecting Early Renal Osteodystrophy.

WORK UNIT NO.: C-2-76

PRINCIPAL INVESTIGATORS: Harvey Gersh, M.D., MAJ, MC
Robert J. Lull, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Daniel A. Nash, Jr., M.D., MAJ, MC; Richard Merrill, M.D., LTC, MC; David B. Olin, M.D., MAJ, MC

OBJECTIVES

1. To evaluate the ability of phosphate scans to diagnose early osteodystrophy.

2. To evaluate the extent and distribution of metastatic calcifications in patients with renal osteodystrophy.

3. To attempt to develop a tool for the evaluation of bone metabolism.

TECHNICAL APPROACH

The patients undergo a six-hour polyphosphate bone scan. The data is computerized and up-take ratios at varying time periods are obtained. The up-take ratio is the measurement of intensity of surrounded soft tissue to that of the femur. Patients are also given different tetracycline drugs orally to label their bones and anterior iliac crest bone biopsy is obtained.

Manpower: None.

Funding:

	FY 76
Consumable Supplies	$632.00

PROGRESS

Nine patients are currently enrolled in the study. Five bone biopsies were obtained with the assitance of the Orthopedic Service, and one biopsy was obtained post mortem. The initial data base is incomplete. Evaluation of the biopsies by Dr. Lent Johnson at AFIP has not been

C-2-76 (continued)

returned to BAMC. When measuring intensity of isotope in soft tissue as compared to the femur, it was found that patients with long-term renal osteodystorphy had scans statistically different from those who had no renal disease or who were short term uremics. Patients who were on dialysis for greater than one year appeared to have an increased bone up-take of the radio isotope as compared to soft tissue. It appears that 4-hour up-take comparisons are a good method for evaluating osteoblastic activity in renal osteodystrophy. When the bone biopsy data are available, we hope to quantitate our scan data using the bone biopsy data as a control. Net changes in bone mass can be easily and painlessly determined by densitometry and if one uses the renal scan to determine osteoblastic activity, it would be possible to derive the rate of osteoclastic activity from these two other limiting parameters. Previously, densitometry studies could give us information concerning absolute changes in renal osteodystrophy, but could not indicate whether these changes were due to changes in osteoblastic activity or osteoclastic activity. The bone scan data are very encouraging and suggest that in combination with densitometry we may have useful clinical tools for evaluating and treating renal osteodystrophy.

The ability of polyphosphate bone scanning as a diagnostic modality for renal osteodystrophy has been evaluated and found to correlate with renal osteodystrophy. These scans are usually positive after one year of hemodialysis. The extent of distribution of metastatic calcification in renal osteodystrophy can be evaluated with these scans, and we have had positive scans in this study, but they do not appear to be clinically important. Bone scans have proven to be an excellent tool for evaluating osteoblastic activity in renal osteodystrophy.

Status: Ongoing.

Presented at the Selected Aspects of Chronic Renal Failure Symposium, 30 January 1976.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Measurement of Lower Esophageal Sphincter Pressure: An Assessment of Perfusion Rate and the Honeywell Model 31 Probe.

WORK UNIT NO.: C-4-76

PRINCIPAL INVESTIGATOR: James E. Gray, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine whether perfusion of the esophageal motility catheter at varying perfusion rates affects the recorded lower esophageal sphincter pressure.

2. To compare lower esophageal sphincter pressures obtained with traditional perfused catheters and with the Honeywell Model 31 probe.

TECHNICAL APPROACH

Our planned approach is to measure the lower esophageal sphincter with varying perfusion rates with the traditional perfused catheter technique and then, in the same patient, to measure the lower esophageal sphinter pressure obtained with the newer self-contained pressure transducers in the Honeywell probe.

Manpower: None.

Funding: None.

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Lactose Intolerance in Mexican American Adults.

WORK UNIT NO.: C-5-76

PRINCIPAL INVESTIGATOR: Eleanor Anne Young, Ph.D.

ASSOCIATE INVESTIGATORS: Ralph F. Wells, M.D., COL, MC
Elliot Weser, M.D., University of Texas Health Science Center

OBJECTIVES

1. To determine the prevalence of lactose intolerance in Mexican-American adults at different age levels.

2. To determine the customary lactose consumption pattern in these adults.

3. To evaluate the usual daily nutrient intake of calories, calcium, protein, and riboflavin of adults with and without lactose intolerance.

TECHNICAL APPROACH

A standard lactose loading test will be performed according to the Protein Advisory Group procedure. A nutritionist will interview each subject to secure an accurate and objective usual daily dietary intake. A standard 24-hour recall procedure will be used for dietary evaluation. Height and weight measurements of each participant will be recorded as well as tricep skinfold and head circumference measurements. Anthropometric measurements will be compared with acceptable norms. Antropometric measurements of subjects with lactose intolerance and without lactose intolerance will be compared. Approximately 500 subjects at different age levels will be evaluated.

Manpower: None.

Funding: None.

PROGRESS

Our participation in this project was quite limited due to the very limited response for volunteers from BAMC. What data was collected,

C-5-76 (continued)

therefore, was turned over to the principal investigator, Eleanor A. Young, Ph.D., and participation in the study at BAMC was terminated.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adequacy of Dialysis with Sorbent-based Dialysate Regeneration System.

WORK UNIT NO.: C-7-76

PRINCIPAL INVESTIGATOR: Daniel A. Nash, Jr., M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Harvey Gersh, M.D., MAJ, MC; Robert P. Bowman, M.D., LTC, MC; Russell W. Steele, M.D., LTC, MC

OBJECTIVES

To evaluate the sorbent based dialysate regeneration system for adequacy of dialysis relative to existing single pass systems.

TECHNICAL APPROACH

Patients were dialyzed with standard hemodialysis equipment, and alternatively, with the sorbent-based dialysate regeneration system. The adequacy of dialysis of the two systems was compared by measuring or observing the clearance data, clinical course, platelet function, and immunological status changes.

Manpower: None.

Funding:

	FY 76
Consumable Supplies	$ 475.00
MEDCASE	$3,980.00

PROGRESS

Four patients have been completely studied, and three others in part. At present, the data is under analysis to consider the need and direction for additional evaluation.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Quantitative Studies of Phagocytosis - the Use of Acridine Orange as an Indicator of Phagocytic Ingestion and Bactericidal Effects.

WORK UNIT NO.: C-9-76

PRINCIPAL INVESTIGATOR: Dennis L. Stevens, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the phagocytosis of polymorphonuclear leukocytes of acridine orange stained bacteria, and to develop a simple, reliable assay of this process which will be amenable to clinical laboratory utilization.

TECHNICAL APPROACH

Acridine orange stained Excherichia coli were fed to human granulocyte suspensions and the fluorescence spectra using 455 Nanometer excitation frequency were performed. A correlation between the alteration in fluorescence spectra and bacterial viability using standard bacteriologic procedures was likewise attempted.

Manpower: None.

Funding:

	FY 76
Consumable Supplies	$549.46

PROGRESS

Bacterial killing by human granulocytes over a 60 minute incubation period has been demonstrated on several occasions with good reproducibility. The change in flurescence spectra from green to red of activated human granulocytes has not been demonstrable due to the insensitivity of the emission photomultiplier tube in the red region.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Antimicrobial Sensitivities of Methicillin Resistant Staphylococci.

WORK UNIT NO.: C-10-76

PRINCIPAL INVESTIGATOR: Adolph E. Rahm, Jr., M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Elwood D. Everett, M.D., LTC, MC; Hugh D. Peterson, M.D., COL, MC; Theodore R. McNitt, M.D., LTC, MC

OBJECTIVES

1. To determine the mean inhibitory concentrations of microtiter technique of 20 strains of methicillin resistant staphylococci to Gentamicin, Tobramycin, Amikacin, Vancomycin and Clindamycin.

2. To determine synergy by killing curves on five strains of methicillin resistant staphylococci with combinations of Vancomycin with Gentamicin, Tobramycin, Amikacin (BBK-8) and Clindamycin.

TECHNICAL APPROACH

Methicillin resistant staphylococcus strains obtained at the Institute of Surgical Research are incubated in wells containing various solutions of antibiotics to determine the concentration at which growth is inhibited. Following determination of inhibitory concentrations, organisms will be incubated with various combinations of antibiotics at subinhibitory concentrations to determine if there is synergism. Syndergism will be determined by performing colony counts on the culture at increasing intervals of time.

Manpower: None.

Funding:	FY 76
Consumable Supplies	$29.45

PROGRESS

There has been considerable difficulty in demonstrating methicillin resistance in the microtiter system. Similar difficulties have been encountered by other investigators and variations in the amount of inoculum, length of incubation, and other factors which may influence the growth of methicillin resistant staphylococci and culture are being evaluated.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Hepatic Failure with an Elemental Diet.

WORK UNIT NO.: C-11-76

PRINCIPAL INVESTIGATOR: Hugh P. McElwee, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Ralph F. Wells, M.D., COL, MC: Melvin L. Butler, M.D., LTC, MC, LAMC; Lawrence F. Johnson, M.D., LTC, MC, WRAMC

OBJECTIVES

To determine if an orally administered elemental diet will speed recovery and/or improve survival from hepatic failure.

TECHNICAL APPROACH

This is a double blind study designed to test the relative effects of different protein diets in patients with liver failure.

Manpower: None.

Funding: None.

PROGRESS

One inpatient with Stage IV hepatic coma verified by abnormal blood ammonia and EEG's was treated with Vivonex at Letterman Army Medical Center under the direction of Dr. Melvin Butler. The coma was resolved and the blood ammonia and EEG's were reverted to normal. This is the only patient studied to date.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Glycerol Lysis Time as a Rapid Screening Measure for Red Cell Membrane Effects.

WORK UNIT NO.: C-15-76

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: John Posch, M.S., DAC

OBJECTIVES

1. To determine normal values of glycerol lysis time.

2. To determine if red cell membrane defects such as thalassemia and spherocytic anemias can be detected out of the range of normal.

3. To statistically evaluate the lysis curve and delineate the best and simplest point for correlating hemolysis to cellular defect.

4. To determine whether this test can be used as a rapid screening measure in a busy hematology clinic.

TECHNICAL APPROACH

Glycerol lysis time using spectrophotometric determination of red cell concentration and comparing with blood sample analyzer various hemoglobinopathies are being performed.

Manpower: None.

Funding: FY 76

Consumable Supplies	$213.15

PROGRESS

Technical evaluation of the protocol and additions to the technical mechanism previously described are undergoing extensive reasearch at this time. Correlation with osmotic fragilities and glycerol lysis time are being made. Correlation with hemoglobinopathies identified by standard hemoglobin electrophoresis and by column chromagoraphy electrophoresis

C-15-76 (continued)

are being performed. Anticipation of adding the capabilities of hemoglobin identification by thermo means and nuclear magnetic resonance methodology are being planned.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Investigation of Methicillin Resistant Staphylococcal Infections.

WORK UNIT NO.: C-16-76

PRINCIPAL INVESTIGATOR: Elwood D. Everett, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: T. R. McNitt, M.D., LTC, MC; A. E. Rahm, Jr., M.D., LTC, MC; D. L. Stevens, M.D., MAJ, MC; H. D. Peterson, D.D.S., M.D., COL, MC

OBJECTIVES

1. To determine the nasal carrier rate of Methicillin resistant Staphylococcus aureus (MRS) in personnel and patients in the burn unit.

2. To assess the point in time and site that burn patients become colonized with MRS (nose, skin, burn wound).

3. To retrospectively determine the attack rate per month of MRS bacteremia during the preceding 12 months.

4. To evaluate the efficacy of Betadine ointment (povidone-Iodine 10%) in the eradication of the nasal carrier rate of MRS in personnel and patients.

5. To determine the attack rate of MRS bacteremia following treatment of nasal carriers of MRS with Betadine ointment.

TECHNICAL APPROACH

The incidence and conrol of MRS among personnel and patients at the burn unit, Ward 14-A, was studied. Since some persons are only transient carriers of staphylococci, an arbitrary period of of nasal cultures once weekly for four weeks was done. In addition, all new admission were cultured daily for four weeks (nose, skin and burn wound) to determine at what site colonization with MRS took place.

Manpower: None.

Funding:

	FY 76
Consumable Supplies	$324.67

C-16-76 (continued)

PROGRESS

Methicillin resistant staphylococci (MRS) are common isolates in the burn unit. All MRS in the survey were phage type 84/85. MRS rarely colonizes healthy hosts but readily colonizes the debilitated burn patient (80% of admissions become colonized) and cause invasive disease (one-third of colonized patients developed serious disease).

Environment is not a significant means of perpetuation of MRS but is likely transferred from a continuing nidus of colonized patients to the new admissions by the hands of employees.

Topical therapy with Betadine did not seem to be a feasible approach to interrupting the outbreak of MRS.

Status: Completed.

Everett, E. D., McNitt, T. R., Rahm, A.E., Stevens, D.L. and Peterson, H.D.: Epidemiologic investigation of methicillin resistant staphylococcus aureus in a burn unit. Submitted to Journal of Infectious Diseases for publication.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects of Cantil Compared with Placebo on Stool Composition and Frequency in Acute Self-Limited Diarrheas.

WORK UNIT NO.: C-18-76

PRINCIPAL INVESTIGATOR: Ralph F. Wells, M.D., COL, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To measure the effect of Cantil on various parameters of stool composition including volume, water content, total solids, electrolytes and transit time.

2. To confirm previous studies which have shown Cantil to be effective in the treatment of acute nonspecific diarrhea.

TECHNICAL APPROACH

Acute nonspecific diarrhea for the purposes of the study will be defined as an acute condition not preceded by a previous bowel disorder of any description. The diarrhea itself shall consist of a sudden increase in the number of watery or semisolid bowel movements to at least three or more in the preceding 8-hour period, usually, but not necessarily, accompanied by abdominal discomfort in the form of pain, cramping or tenderness. In addition, the diarrhea itself must be self-limited; i.e., those patients whose diarrhea has not diminished by 50% or more within four days will be excluded from analysis.

Patients who meet these criteria and who also meet the other inclusion and exclusion criteria of the study will be given their medication in tablet form, consisting of either Cantil, Lotmotil, or placebo. Patients will be assigned their medication according to a randomization table kept in the pharmacy which will designate their treatment according to time of entry into the study.

Manpower: None.

Funding: None.

C-18-76 (continued)

PROGRESS

No progress has been made. This project was approved at a joint meeting of the Army Investigation Drug Review Board, Clinical Investigation Committee, and Human Use Committee on 16 December 1975. However, final approval by The Surgeon General was held in abeyance until it was determined if non-active duty volunteers would be responsible for hospital charges incurred while participating in the study. After careful review, the Gastroenterology Service has elected not to initiate the study.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Value of Antacid Therapy in Treatment of Duodenal Ulcers.

WORK UNIT NO.: C-19-76

PRINCIPAL INVESTIGATOR: Hugh P. McElwee, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: James E. Gray, M.D., MAJ, MC; Ralph F. Wells, M.D., MAJ, MC; Melvin L. Butler, M.D., LTC, MC, LAMC; Staff, LAMC; Staff, WBAMC; Staff, WRAMC

OBJECTIVES

To determine the efficacy of antacid therapy in duodenal ulcer disease.

TECHNICAL APPROACH

To test the effectiveness of antacids on the healing rate of duodenal ulcers. This is a double blind study comparing antacids vs. placebo. All patients will be diagnosed and followed by oral endoscopy to monitor response.

Manpower: None.

Funding: None.

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Therapeutic and Diagnostic Role of Air Calorics.

WORK UNIT NO.: C-22-76

PRINCIPAL INVESTIGATOR: Michael Polsky, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Carl H. Gunderson, M.D., COL, MC
Richard Calkins, M.D., LTC, MC

OBJECTIVES

To develop a device for the determination of the possible therapeutic and diagnostic role of air calorics.

TECHNICAL APPROACH

The device in question would be a modified portable hot air blower. Air would flow through a tube connected to an ear-plug of the sort used in transister radio. Since the surface to be contacted is the tympanic membrane, the flow of air need not be rapid, and conceivably the system will not require a fan. The system should incorporate a thermostat rendering possible adjustments between 37^{o} and 44^{o} C.

Manpower: None.

Funding: None.

PROGRESS

Prototype apparatus is under construction; completed model has not been received.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Demonstration of a Testosterone Binding Protein in Semen.

WORK UNIT NO.: C-23-76

PRINCIPAL INVESTIGATOR: Albert Thomason, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To demonstrate a testosterone binding protein in semen.

TECHNICAL APPROACH

An attempt is being made to demonstrate a testosterone binding protein in semen by showing that a protein traversing polyacrylamide gel in an electrophoresis apparatus will concentrate labelled testosterone.

Manpower: None.

Funding: None.

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Use of Teichoic Acid Antibodies in Diagnosing Serious Staphylococcal Disease in Burn Patients.

WORK UNIT NO.: C-25-76

PRINCIPAL INVESTIGATOR: Theodore R. McNitt, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Elwood D. Everett, M.D., LTC, MC; D. L. Stevens, M.D., MAJ, MC

OBJECTIVES

1. To determine if teichoic acid antibody titers change in a diagnostic fashion in burn patients with staphylococcal infections.

2. To compare teichoic acid antibody titers in patients with methicillin sensitive and methicillin resistant staphylococcal infections.

3. To correlate teichoic acid antibody titers in burn patients with the degree of staphylococcal disease.

TECHNICAL APPROACH

Serial blood samples from thermally injured patients will be obtained and teichoic acid antibodies titers will be measured by immunodiffusion assay after the method of Crowder and White.

Manpower: SP5 (2 months)

Funding:

	FY 76
Consumable Supplies	$360.00

PROGRESS

Fifty patients have been entered into the study. The blood samples are currently being evaluated for the level of teichoic acid antibody.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Vagal Stimulation on Canine Plasma Histamine Levels and Mast Cell Degranulation.

WORK UNIT NO.: C-26-76

PRINCIPAL INVESTIGATOR: Charles B. Brearley, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine if elevations of arterial blood histamine occur in anesthetized dogs following unilateral and bilateral vagal stimulation.

2. To determine the extent of mast cell degranulation in the lungs of anesthetized dogs following bilateral vagal stimulation.

TECHNICAL APPROACH

Dogs weighing approximately 15 kg are anesthetized with pentobarbital, 25 mg/kg I.V.; they are intubated and ventilated with Bird Mark VII ventilator to keep arterial pH and PCO_2 in the physiologic range and to keep arterial CO_2 approximately 200 mm Hg. The right femoral artery is cannulated and attached to a Statham pressure transducer and E for M Recorder which records continual blood pressures and heart rates. Central venous line is inserted via the right external jugular vein into the right atrium for administration of fluids for withdrawing blood samples. The right and left vagosympathetic nerve trunks are exposed and attached to a nerve stimulator set at 5 volts, 1.5 millisecond pulse duration and 12 pulses per second. An esophageal balloon is inserted and connected to a pressure transducer to record changes in intrathoracic pressure, and a pneumotachograph is inserted in line with the patient's breathing apparatus, so that continuous flow rates can be monitored. Flows are integrated on the E for M recorder to give volumes. Following initial blood samples for arterial blood gases and arterial and venous histamine levels, and following baseline ventilatory volume, pressure and flow measurements, one minute of electrical stimulation is carried out with continual ventilatory measurements as well as simultaneous arterial and venous samples for histamine at/immediately following stimulation, and at 2-minute, 5-minute, and 10 minute intervals. The catheters are then removed and the surgical wounds closed.

Manpower: None.

Funding: None.

C-26-76 (continued)

PROGRESS

Five dogs have undergone the above mentioned procedure. Although significant rises in airway resistance have been noted following bilateral vagal stimulation, plasma and whole blood histamine levels have not changed significantly from baseline. These findings could indicate one of three things: (1) Vagal stimulation was not satisfactory; this is unlikely because of the patient's heart rate response and elevated airways resistance measurements. (2) Vagal stimulation alone does not cause mediator release. (3) Vagal stimulation as mentioned previously in the protocol may simply enhance IgE mediated release of vasoactive and bronchoactive substances. This possibility will be investigated subsequently by sensitizing several dogs to ascaris suum inhaled antigen, following which arterial histamine levels will be drawn. Vagal stimulation will subsequently be done to see if enhancement of IgE mediated release of vasoactive substances occurs following vagal stimulation.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Pilot Study: Evaluation of Nasogastric Hyperalimentation and Peripheral Venous Hyperalimentation in Cancer Patients.

WORK UNIT NO.: C-27-76

PRINCIPAL INVESTIGATOR: Richard A. Shildt, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To gather data on two forms of hyperalimentation: nasogastric hyperalimentation and peripheral venous hyperalimentation and compare the results with a control group receiving an oral diet. This is a pilot study to determine the feasibility of hyperalimentation on the Oncology Service.

TECHNICAL APPROACH

Patients seen by the Oncology Service who are to begin chemotherapy and who have lost at least 10% of their body weight normally recorded in the pre-illness period, or who have albumin less than 8 mg%, will be asked to participate in the study.

Patients will be randomized into three groups. Calorie counts will be done on each group. A maximum of 24 patients, 8 in each group, will be studied. Group A will be the control group receiving a diet outlined by the dietician. Group B will receive a diet outlined by the dietician and nasogastric hyperalimentation with Ensure. Group C will receive a diet outlined by the dietician and peripheral venous hyperalimentation with Intralipid and Freamine.

Manpower: None.

Funding: None.

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Prevalence of HBS Antigen, Carrier State and HBS Antibody in Gastroenterologists. (El Paso Study).

WORK UNIT NO.: C-29-76

PRINCIPAL INVESTIGATOR: Hugh P. McElwee, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: James L. Stammer, M.D., MAJ, MC
Ralph F. Wells, M.D., COL, MC

OBJECTIVES

To determine the prevalence of HBS antigen carrier state and HBS antibody in physicians practicing gastroenterology.

TECHNICAL APPROACH

At the recent William Beaumont Symposium on Gastrointestinal Diseases, we collected blood samples from endoscopists. We also collected demographic data from each volunteer. We tested each blood sample for the presence or absence of hepatitis surface antigen and hepatitis surface antibody.

Manpower: None.

Funding: None.

PROGRESS

This was a pilot project to precede the major collection of samples at the AGA meeting in Miami in May 1976. There were 139 registrants at the William Beaumont Symposium, and 36 blood samples were collected. Thirty-four were from endoscopists. This represented 24.8% volunteer collection rate; however, the percent collection rate is probably higher as only about 75 to 100 of the registrants were endoscopists. This adjustment makes our true collection rate between 35 and 45%.

C-29-76 (continued)

Antigen and antibody testing showed all 34 samples were negative for hepatitis associated antigen whereas three of 34 (8.8%) of the samples were positive for hepatitis surface antibody. Correlation with demographic data is not yet complete. Since the anticipated rate of hepatitis surface antigen positivity is approximately 1%, the negative results in 34 samples is not surprising. The anticipated rate of hepatitis surface antibody positivity is about 12%, and our findings are compatible. We are unable to draw meaningful conclusions with regard to the prevalence of hepatitis markers from this limited study.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Prevalence of HBS Antigen, Carrier State, and HBS Antibody in Gastroenterologists. (Miami study of physicians attending AGA Meeting).

WORK UNIT NO.: C-30-76

PRINCIPAL INVESTIGATOR: Hugh P. McElwee, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: James L. Stammer, M.D., MAJ, MC
Ralph F. Wells, M.D., COL, MC

OBJECTIVES

To determine the prevalence of HBS antigen carrier state and HBS antibody in physicians practicing gastroenterology.

TECHNICAL APPROACH

Blood samples will be drawn from endoscopists attending the American Gastroenterological Association meeting in Miami, Florida. Each blood sample will be tested for the presence or absence of hepatitis surface antigen and hepatitis surface antibody. Demographic data will be obtained from each volunteer.

Manpower: None.

Funding:

	FY 76
Consumable Supplies	$ 86.38
Contractural Services	$720.00

RESULTS

Blood samples were collected at the AGA meeting in Miami in May 1976. Samples are in the process of being evaluated.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Systemic Mast Cell Disease with Cimetidine (SK&F 92334).

WORK UNIT NO.: C-33-76

PRINCIPAL INVESTIGATOR: Ralph F. Wells, M.D., COL, MC
Joe A. Dean, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To measure the effect of Cimetidine, a selective H^+ blocking agent, on recurrence of gastric ulceration, intestinal hemorrhage, pruritus and diarrhea in a patient with known systemic mast cell disease.

TECHNICAL APPROACH

The patient will be treated under the Smith, Kline and French Protocol #D01 for Cimetidine (SK&F 92334) as treatment of a special case. Under this protocol, only those seriously patients in whom reduction of gastric acid output may be required for their treatment and when no alternative therapy is available or included may be entered. Each patient will be studied on a regimen of 300 mg. q.i.d. administered with meals and h.s. Should this not completely alleviate symptoms, the dosage may be increased. Antacids may be administered p.r.n.

Manpower: None.

Funding: None.

PROGRESS

This is a new project.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Effect of Hyperbaric Carriers on the Distribution of Aminoglycoside Antibiotics in the Cerebrospinal Fluid of Dogs.

WORK UNIT NO.: C-35-76

PRINCIPAL INVESTIGATOR: Elwood D. Everett, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Christopher Chaput, M.D., MAJ, MC: Thomas Rankin, M.D., MAJ, MC; Theodore R. McNitt, M.D., LTC MC; Adolf Rahm, M.D., LTC, MC; Dennis L. Stevens, M.D., MAJ, MC

OBJECTIVES

To determine the effect of hyperbaric (10% dextrose) solutions on the distribution of intrathecally administered aminoglycoside antibiotics.

TECHNICAL APPROACH

Two adult mongrel dogs will have an Ommaya reservoir placed in their lateral ventricles. This will be the site for sampling of ventricular fluid during the period of antibiotic administration. 10 mg of gentamicin or tobramycin or 20 mg of Amikacin dissolved in 5 cc D10% dextrose (for hyperbaric phase) or 5 cc sterile water (non-hyperbaric phase). This will be injected at the lumbar level. The animal will then be placed in 30° Trendelenberg position. An initial sample of spinal fluid will be obtained prior to any antibiotic administration. Cell count with differential, sugar and protein determinations and antibiotic activity will be done on this sample. Subsequent to the antibiotic administration, 1 cc samples will be removed from the lumbar, cisternal and ventricular sites at 10, 30, 60, 120, 240, 480, 960, and 1800 seconds. These will be assayed for antibiotic concentrations. Gentamicin and tobramycin concentrations will be measured by radioimmunoassay. Amikacin levels will be measured by a microbiologic assay using a resistant providence strain.

Manpower: None.

Funding: None.

PROGRESS

This is a new project.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cefazolin as a Prophylactic Antibiotic in Vaginal Hysterectomy.

WORK UNIT NO.: C-37-74

PRINCIPAL INVESTIGATOR: Willie J. Lett, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Barry L. Davison, M.S., CPT., MSC; Rudi Ansbacher, M.D., COL, MC; Warren N. Otterson, M.D., COL, MC

OBJECTIVES

To compare the effectiveness of one dose of cefazolin to three doses of cephaloridine as a prophylactic antibiotic in vaginal hysterectomy.

TECHNICAL APPROACH

One hundred fifty six patients undergoing vaginal hysterectomy with or without anterior and/or posterior repair, and/or BSO, were by random selection placed into three groups. One group received one gram of Loridine preoperatively, immediately postoperatively, and 12 hours postoperatively. One group received one gram of Kefzol one hour preoperatively only. One group received no medication. Forty-nine patients received Loridine, fifty-five patients received Kefzol, and fifty-two patients received no medication.

All groups had a gram of posterior vaginal cuff taken at the time of operation for aerobic and anaerobic cultures. They also had pre- and postoperative SMA-18 performed. Their hospital courses were recorded based on the presence or absence of febrile morbidity as described in the original protocol.

Total follow-up included one to two days preoperatively to six weeks postoperatively.

Manpower: None.

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$0.00	$ 150.00	$1,064.99
MEDCASE	$0.00	$2,433.46	

C-37-74 (continued)

PROGRESS

The Loridine group had 8% febrile morbidity, the Kefzol group 9% febrile morbidity, and the control group 58% febrile morbidity. The predominant organism was Beta Hemolytic Streptococcus Group D for the aerobes and Bacterioides melaninogenicus species for the anaerobes.

Conclusions: One gram of Kefzol, one hour preoperative, is a safe and effective method of prophylactic antibiotic in vaginal hysterectomy. Our study shows that the realm of prophylactic antibiotic is definitely in the preoperative time period, and use of antibiotics for periods longer than the day of surgery is not necessary and may result in the development of strains of organisms unfamiliar and resistant to therapy.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Laminaria: Two Outpatient Uses.

WORK UNIT NO.: C-38-74

PRINCIPAL INVESTIGATOR: Jose R. Ossorio, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., COL, MC
Warren N. Otterson, M.D., COL, MC

OBJECTIVES

To determine if by the use of laminaria tents, sufficient dilatation of the cervix can be obtained in patients with stenotic or tight cervical ossa, so as to enable easier endometrial sampling by endometrial biopsy or jet washing and easier insertion of intrauterine device in nulliparous patients.

TECHNICAL APPROACH

A small thin laminaria for slow dilatation of the cervix was inserted in patients with cervical stenosis. This laminaria was removed in three to four hours. Endometrial biopsy was done on all patients and on some, a Vabra aspiration was also performed. The subjective symptoms of the patients at the time of insertion, at the time of dilatation, and at the time of removal were recorded. The physician's impressions on the easiness or difficulty to do the insertion and removal of laminaria were also recorded.

Manpower: None.

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$0.00	$0.00	$330.00

PROGRESS

A total of 26 patients underwent laminaria insertion in a period of two years. Only one patient complained of severe cramping at the time of insertion; the rest complained only of mild cramping at that time. At the time of removal patients complained only of mild cramping.

C-38-74 (continued)

All physicians agreed on the easiness of the laminaria insertion, removal of the laminaria and of doing the endometrial sampling that followed. In all 26 patients the specimen obtained had adequate material for pathological evaluation. No failures occurred.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Relationships of Vaginal and Cervical Flora in Pregnancy and Premature Rupture of Membranes.

WORK UNIT NO.: C-11-75

PRINCIPAL INVESTIGATOR: James E. Connerth, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Willie J. Lett, M.C., MAJ, MC; Warren N. Otterson, M.D., COL, MC; Rudi Ansbacher, M.D., COL, MC; Barry L. Davison, M.S., CPT, MSC

OBJECTIVES

To assess the possible degree of correlation between vaginal and cervical flora in pregnancy and premature rupture of membranes.

TECHNICAL APPROACH

Vaginal and cervical cultures are obtained on new prenatal patients during the first and third trimester of pregnancy. Cultures (anaerobic and aerobic) are repeated at the time of premature rupture of membranes.

Manpower: None.

Funding:	FY 76	FY 75
Consumable Supplies	$2,200.00	$4,099.81

PROGRESS

Initial phase of the study is completed. Efforts are now directed toward collecting a group of patients out of those initially cultured with premature rupture of membranes. The anaerobic culture system is showing recovery of organisms.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Correlation of Phenotypic Sex of Fetuses with Amniotic Fluid Testosterone Levels.

WORK UNIT NO.: C-20-75

PRINCIPAL INVESTIGATOR: William Sutherland, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., COL, MC; Edward D. Helton, Ph.D., CPT, MSC; Harris D. Plant, SP4

OBJECTIVES

1. To determine whether testosterone levels in male fetuses, 16-20 weeks embryonic age are significantly higher than those of female fetuses.

2. To determine whether the observed ranges of testosterone values will allow one to deduce phenotypic sex from the value of amniotic fluid testosterone.

TECHNICAL APPROACH

Fifty patients undergoing elective second trimester abortions at Brooke Army Medical Center over a six month period will be surveyed. Amniotic fluid will be obtained at the time an appropriate abortifacient is injected into the amniotic cavity. Assay for testosterone will be performed utilizing a method which incorporates procedural details set forth by Armando de la Pena (laboratory method), Burton V. Caldwell (laboratory notes on radioimmunoassay of steroids) and Hillier, Bronsey and Cameron with only slight modification by Helton and Plant for use with liquor amnii. Following abortion, fetal sex will be determined anatomically by at least two physicians, including one of the investigators. Ideally, one might determine the chromosomal complement of every aborted fetus, but this is not economically feasible. Discrepancies between phenotypic and genetic sex occur so rarely that statistical correlations are unlikely to be invalidated. Fetuses in which maceration precludes anatomical sex determination will be excluded from this investigation.

Manpower: SP4 (4 months)

Funding:	FY 76	FY 75
Consumable Supplies	$285.00	$436.79

C-20-75 (continued)

PROGRESS

Determinations of testosterone in amniotic fluid have been tabulated in early specimens. However, there has been poor correlation with phenotypic sex. There have been alterations in the basic RIA protocol and later specimens are being run to see if correlation can be improved. Alterations in the RIA protocol appear to reflect a more exact determination of testoserone in amniotic fluid.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Decision to Obtain Voluntary Sterilization

WORK UNIT NO.: C-1-76

PRINCIPAL INVESTIGATOR: Margaret Clark

ASSOCIATE INVESTIGATORS: Rudi Ansbacher, M.D., COL, MC
Warren N. Otterson, M.D., COL, MC

OBJECTIVES

To study the determinants of choice of male versus female sterilization procedures. To evaluate postoperative satisfaction with the operation of choice in terms of these factors.

TECHNICAL APPROACH

A self-completion questionnaire has been given to individuals who come to the Department of Obstetrics and Gynecology and to the Department of Urology seeking information and counseling regarding voluntary sterilization. A follow-up questionnaire has been mailed to consenting individuals approximately six months after a sterilization procedure.

Manpower: None.

Funding: None.

PROGRESS

As of 15 April 1976, one hundred eighty three sets of preoperative questionnaires had been completed in the two clinics. Sixty-eight were done in the Urology Clinic and one hundred fifteen were done in the sterilization clinic run by the Department of Ob-Gyn. Study is continuing to increase sample size. Forty-three individuals had completed the follow-up questionnaries.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Spinal Cord Injuries: Sperm Antibodies.

WORK UNIT NO.: C-3-76

PRINCIPAL INVESTIGATOR: Rudi Ansbacher, M.D., COL, MC

ASSOCIATE INVESTIGATOR: Mauro P. Gangai, M.D., COL, MC

OBJECTIVES

To determine the incidence of sperm-agglutinating and sperm-immobilizing antibodies in the sera of 25 men after spinal cord injuries.

TECHNICAL APPROACH

Men hospitalized with spinal cord injuries or those seen in the Urology Clinic, BAMC, have a sexual history taken to determine the frequency of erections, seminal emissions, and sexual history prior to and subsequent to their injury. Ten milliliters of blood are drawn from each man, the serum is removed from the clotted blood by centrifugation, complement is destroyed by heating the serum for 30 minutes at 58° Celsius, and the serum samples are stored at below -25° Celsius until and between testing days.

The macroscopic gelatin sperm-agglutination and the sperm-immobilization test are utilized to determine the presence of circulating sperm antibodies, using pooled rabbit serum as the complement source and normal semen samples obtained from donors with at least 60 million spermatozoa per milliliter and motility above 70 percent as the antigen.

Results will be correlated with each man's history and compared to previously obtained data from men studied before and after bilateral vas ligations.

Manpower: None.

Funding: None.

C-3-76 (continued)

PROGRESS

Due to lack of support from the Rehabilitation Unit of the Veterans Administration Hospital, San Antonio, Texas, all men entering this study are coming from the population seen at BAMC.

To date, seven have been studied: the spinal cord injuries occurred between 4 and 26 years prior to interview. Their ages ranged from 21-47 years. None have had circulating sperm-agglutinating or sperm-immobilizing antibodies.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Cellular Immunity to the Varicella-Zoster Virus Employing a Newly Developed Microassay Technique.

WORK UNIT NO.: C-14-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To examine the applicability of a newly developed microassay technique which measures cellular immunity, specific to the Varicella-Zoster virus.

TECHNICAL APPROACH

Assays of Varicella-Zoster induced lymphocyte blastogenesis were accomplished with methods similar to those employed for a one way mixed lymphocyte culture. Stimulating cells include tissue culture cells persistently infected with Varicella-Zoster virus and uninfected culture cells. Counts per minute for lymphocytes incubated with the infected cells divided by counts per minute following incubation with uninfected cells determined the blastogenic index and a value of 3 or greater is considered positive in most assays. This assay has been extended to include other infectious agents including herpex simplex virus Type I, herpes simplex virus Type II, rubella virus, measles virus, cytomegalic virus, influenza virus, and Sporothrix schenckii.

Manpower: None.

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$2,617.10	$1,112.50	$165.20
Capital Equipment		$ 695.00	
Reprints	$ 76.00	$ 134.65	
TDY		$ 397.00	

PROGRESS

The development of cell-mediated immunity by ^{51}Cr lymphocytotoxicity was measured over a 42-day period in 12 children immunized with live

C-14-74 (continued)

rubella virus vaccine (HPV-77-DE5) and was compared with the development in serum of hemagglutination inhibition antibody response to rubella. Cell-mediated immunity was detected as early as three days after immunization, reached a maximum between 7 and 14 days, and declined slowly thereafter. Serum antibody was not detected until more than 14 days, and declined slowly thereafter. Serum antibody was not detected until more than 14 days after immunization, and then it gradually increased. Two control children remained negative for both tests. An additional six children within the same age group, who presumably had been immunized or infected with rubella previously, had appreciable titers for cell-mediated immunity and hemagglutination inhibition. In comparing the immune responses according to birthweights, cell-mediated immunity was detected earlier in infants who were born at full term (>2,500 g) than in those of low birthweight. A similar, but less striking, difference was the earlier development of humoral antibody in the full-term infants. The measurements of specific cell-mediated immunity to rubella virus by lymphocytotoxicity may provide a valuable in vitro marker of effectiveness of vaccine and of protective immunity to viral infection.

Status: Ongoing.

Steele, R.W., Fuccillo, D.A., Hensen, S.A., Vincent, M.M. and Bellanti, J.A.: Specific inhibitory factors of cellular immunity in children with subacute sclerosing panencephalitis. J. Pediat. 88:56-62, 1976.

Steele, R.W., Cannady, P.B., Jr., Moore, W.C., Jr. and Gentry, L.O.: Cellular immunity to sporothrix schenckii, J. Clin. Invest. 57:156-160, 1976.

Steele, R.W., Sieger, B.E. and Gentry, L.O.: Therapy for disseminated coccidioidomycosis with transfer factor from a related donor. Amer. J. Med. (In Press).

Steele,R.W., Suttle, D.E., LeMaster, P.C., Patterson, F.D., and Canales, L.: Screening for cell-mediated immunity in children. Amer. J. Dis. Chi.d (In Press).

Steele, R.W., et al: Transfer factor, basic properties in clinical applications (Ed. Ascher, M.S., Gottlieb, A.A., Kirkpatrick, C.H.) Animal models of transfer factor. Academic Press, New York, 1976.

Steele, R.W., et al: Transfer factor, basic properties in clinical applications (Ed. Ascher, M.S., Gottlieb, A.A., Kirkpatrick, C.H.) Transfer of cellular reactivity to 3 non-human primate species with human and baboon transfer factor. Academic Press, New York, 1976.

C-14-74 (continued)

Steele, R.W., et al.: Transfer factor, basic properties in clinical applications (Ed. Ascher, M.S., Gottlieb, A.A., Kirkpatrick, C.H.) Prevention of herpes simplex virus Type I fatal dissemination in primates with human transfer factor. Academic Press, New York, 1976.

In vivo transfer of cellular immunity to primates with transfer factor prepared from human or primate leukocytes. Presented at the Second Workshop on Basic Properties and Clinical Applications of Transfer Factor, Fort Dietrick, Maryland, October 1975.

This project was awarded the Eighth Ogden Bruton Award at the 11th Annual Uniformed Services Pediatric Seminar, Norfolk, Virginia, 14-18 March 1976.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cellular Immunity to Herpesvirus Hominis in the Compromised Host.

WORK UNIT NO.: C-15-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To develop specific and reliable in vitro assays of both the afferent and efferent mechanisms of cellular immunity to Herpes virus hominis (HVH) and to examine responses of patients with malignant disease or of patients on immunosuppressive therapy.

TECHNICAL APPROACH

A ^{51}Cr lymphocycotoxicity microassay to cell lines persistently infected with HSV-1, HSV-2 or V-Z is being used in the studies. Briefly, this technique examines lymphocyte-target cell interaction employing the infected cell lines as target cells. The quantitative release of ^{51}Cr from the target cells is used as an index of lymphocyte mediated reactivity against the infected cells. Uninfected tissue cultures serve as controls to quantitate ^{51}Cr release not attributed to the virus itself. Specific immune release of 8% or greater is considered positive in these assays.

Manpower: None.

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$2,141.50	$ 504.00	$1,206.78
TDY			$ 492.99
Reprints	$ 130.55		

PROGRESS

Cellular immunity to herpes simplex virus type 1 (HSV-1) in 12 volunteers with recurrent herpes labialis was evaluated by means of two microassays.

C-15-74 (continued)

In the blastogenesis assay, lymphocytes were incubated with tissue culture cells persistently infected with HSV-1. Uninfected cells were used as controls and a blasogenic index was calculated. The mean blastogenic index (±SD) for subjects with recurrent herpes labialis was 26.9 (±8.3); the mean blastogenic index (±SD) in control donors with antibody to HSV-1 was 13.4 (±7.2). The difference between these values was statistically significant ($t = 4.154$; $P < 0.001$). In the cytotoxicity assay, cells of the same persistently infected line were used as target cells, and release of ^{51}Cr from these cells or from control cells served as the index of lymphocyte reactivity. Specific immune release attributable to HSV-1 averaged 3.7% (±1.8%) in subjects with recurrent herpes labialis, compared with 23.1% (9.8%) in controls ($t = 6.135$; $P < 0.001$). These data suggest a dissociation between mechanisms of cellular immunity, with enhanced lymphocyte blastogenesis but decreased toxicity. Recurrent herpes labialis may thus result from subtle cellular immune deficiency involving at least one of the efferent mechanisms.

Status: Ongoing.

Steele, R.W., Britton, H.A., Anderson, C.T. and Kniker, W.T.: Severe combined immunodeficiency with cartilage-hair hypoplasia: in vitro response to thymosin and attempted reconstitution. Rediat. Res. 10:555, 1976.

Steele, R.W., Fuccillo, D.A., Hensen, S.A., Vincent, M.M. and Bellanti, J.A.: Cellular immunity and SSPE. Arch. Neurol. 32:488-504, 1975.

Steele, R.W.: Subacute sclerosing panencephalitis. J. Pediat. (In press) 1976.

Steele, R.W., Keeney, R.E., Brown, J., III and Young, E.J.: Cellular immune responses to herpes group viruses during treatment with adenine arabinoside. Submitted for publication.

Cellular immune responses to herpes group viruses during treatment with adenine arabinoside. Presented at the Spring 1976 meeting of the Pediatric Societies. St. Louis, Mo.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Preparation and Purification of Dialyzable Transfer Factor for the Treatment of Selected Infectious Diseases.

WORK UNIT NO.: C-42-74

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Hobert L. Pence, M.D.
Luis Canales, M.D., COL, MC

OBJECTIVES

To evaluate the efficacy of transfer factor therapy for disseminated fungal or viral disease or tuberculosis unresponsive to the usual forms of therapy.

TECHNICAL APPROACH

Dialyzable transfer factor (TF_d) was prepared and purified from donors by the methods of Lawrence and Al-Askari. In most cases, leukocytes have been obtained by leukapheresis using a continuous-flow celltrifuge (American Instrument Co.). Lymphocytes are separated from the cell pack using a Hypaque-Ficoll gradient, freeze thawed in the presence of DNase 10 times and TF was then dialyzed and concentrated by lyophilization. All recipients of human transfer factor are first tested for skin test and blastogenic responses to the antigens under investigation at which time, transfer factor is injected subcutaneously in the dose equivalent to 1×10^9 lymphocytes. Three days after injection, skin tests are usually repeated and blood is again drawn for *in vitro* study.

Manpower: None.

Funding:	FY 76	FY 75	FY 74
Consumable Supplies	$2,818.30	$1,331.00	$1,092.41

PROGRESS

A 17-year-old Caucasian female who developed disseminated coccidioidomycosis with culture positive meningitis during her third trimester of pregnancy was treated with amphotericin B and subsequently

C-42-74 (continued)

with transfer factor prepared from her father's peripheral lymphocytes. Clinical response and *in vivo* and *in vitro* immunologic data indicated that this transfer factor afforded a significant contribution to her survival while previous therapy with transfer factor from an unrelated donor provided only transient immunologic reactivity. This experience suggests that transfer factor prepared from a related donor with positive responses to *C. immitis* may be more efficacious than that prepared from an unrelated donor.

Status: Ongoing.

Steele, R.W., Sieger, B.E., McNitt, T.R., Moore, W.L., Jr. and Gentry, L.O.: Therapy for disseminated coccidioidomycosis with transfer factor from a related donor. Amer. J. Med. (In press) 1976.

Steele, R.W., Eichberg, J.W., Heberling, R.L., et al: In vivo transfer of cellular immunity to primates with transfer factor prepared from human or primate leucocytes. Cell. Immunol. 22:110-120, Mar 1976.

Steele, R.W., Britton, H.A., Anderson, C.T. and Kniker, W.T.: Severe combined immunodeficiency with cartilage-hair hypolasia: in vitro response to thymosin and attempted reconstitution. Pediat. Res. 10: 555, 1976.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: A Comparison of Immunologic Parameters in Three Nonhuman Primates.

WORK UNIT NO.: C-19-75

PRINCIPAL INVESTIGATOR: Russell W. Steele, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: William T. Kniker, M.D.
Seymour S. Kalter, Ph.D.

OBJECTIVES

To undertake a detailed analysis of host herpes virus interaction in nonhuman primates in an effort to find factors in each of three species of nonhuman primates which are most critical to defense against infectious and oncogenic agents.

TECHNICAL APPROACH

Present studies have evaluated 3 primate species (baboons, cebus monkeys and marmosets) with various parameters of phagocytic, humoral and cell-mediated immune responses. Such assays have included cytotoxicity, lymphocyte blastogenesis, and lymphokine production as parameters of cellular immunity; chemotaxis, phagocytosis, bactericidal capacity of neutrophils, and antibody production to various antigens. In vivo responses of skin graft rejection, skin test reactivity and response to thymosin, transfer factor, and thymus transplants have also been investigated.

Manpower: None.

Funding:	FY 76	FY 75
Consumable Supplies	$1,215.87	$2,750.11
Reprints	$ 121.61	

PROGRESS

Dialyzable transfer factor (TF_d) prepared from a human donor and transfer factor (TF) from baboon whole cell lysates was administered to three species of nonhuman primates: baboons, cebus monkeys and

C-19-75 (continued)

marmosets. In vivo transfer was evaluated with in vivo skin test and in vitro blastogenic responses to multiple antigens. Transfer of cellular reactivity in all three nonhuman primate species was demonstrated with both human TF_d and baboon TF. A cumulative conversion rate of 45% for skin test responses and 65% for lymphocyte blastogenesis was demonstrated following human TF_d injection while conversion was 17% and 33% respectively following baboon TF. Specificity was supported by the absence of conversion to TF donor negative antigens. There were no significant differences observed between the three recipient primate species.

Subsequently, human transfer factor was administered to two baboons and a chimpanzee who were raised in germ free environments. In vitro blastogenic assays prior to TF administration confirmed noreactivity to the multiple antigens but skin tests were not performed so that presensitization or exposure to the antigens was avoided. Subsequent skin test and blastogenic responses were strongly positive indicating that antigen exposure is not necessary for transfer of reactivity with TF.

Status: Ongoing.

Macias, E.G., Steele, R.W., McCullough, B., et al: Cell-mediated immunity fungal, bacterial, viral, and chemical antigens in three nonhuman primates. Presented at the Federation meetings April 1975. Fed. Proc. 34:824, 1975.

Steele, R.W., Eichberg, J.W., Rommel, F.A., et al: E and EAC Rosettes in man and nonhuman primates and the effect of thymosin in vitro. Presented ath the Federation meetings April 1975. Fed. Proc. 34:966, 1975.

Steele, R.W., Eichberg, J.W., Heberling, R.L., et al: Mixed lymphocyte reactivity and skin graft rejection in nonhuman primates. (In press) J. Med. Primatol. 1976.

Steele, R.W., Eichberg, J.W., Heberling, R.L., et al: In vivo transfer of cellular immunity to primates with transfer factor prepared from human or primate leucocytes. Cell. Immunol. 22:110-120, Mar 1976.

Kalter, S.S., Steele, R.W., et al: Immunological aspects of herpesvirus infections in primates. Oncogenesis and herpesvirus II, de-The, G., Epstein, M.A. and zur Hausen, H. ed., Lyon, IARC Scientific Publications, 1975.

C-19-75 (continued)

Steele, R.W., Eichberg, J.W., Heberling, R.L., et al: Animal models of transfer factor. In Transfer Factor, Basic Properties and Clinical Applications, Academic Press, New York, 1976.

Steele, R.W., et al: Prevention of herpes simplex virus type 1 fatal dissemination in primates with human transfer factor. In Transfer Factor, Basic Properties and Clinical Applications, Academic Press, 1976.

Eichberg, J.W., Heberling, R.L., Steele, R.W., Kniker, W.T. and Kalter, S.S.: Transfer factor to prevent herpes virus infection. Fed Proc (In press) 1976.

Eichberg, J.W., Steele, R.W., et al: Chemotaxis and phagocytosis in nonhuman primates. (Submitted for Publication)

Eichberg, J.W., Steele, R.W., Kalter, S.S., et al: Cellular immunity in pnotobiotic primates induced by transfer factor. Cell. Immunol. (In press) 1976.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Use of Growth Hormones in Hypopituitary Patients.

WORK UNIT NO.: C-12-76

PRINCIPAL INVESTIGATOR: Adrienne B. Butler, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: K. James Ehlen, M.D., MAJ, MC; Stephen R. Stephenson, M.D., CPT, MC; Luis Canales, M.D., COL, MC

OBJECTIVES

To investigate the growth response in hypopituitary patients to commercially available human growth hormone.

TECHNICAL APPROACH

Human growth hormone, CB 311, is being given in a dose of 2 units three times weekly to one patient who is 8 years post excision of a craniopharyngioma.

Manpower: None.

Funding:

	FY 76
Consumable Supplies	$1,600.00

PROGRESS

HGH was initiated 25 January 1976. As of 3 April 1976, the patient had grown 1 inch in height, gained one shoe size and shown some redistribution of body fat and maturing facies. There have been no untoward effects.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects on Attendees of a Course in Human Sexuality.

WORK UNIT NO.: C-34-74

PRINCIPAL INVESTIGATOR: Harry A. Croft, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Gilbert R. Kaats, Ph.D., LTC, USAF
Edwin Cornelius, CPT MSC

OBJECTIVES

To study the existence of and extent of change in attendees of a course in human sexuality in regards to sexual attitudes, beliefs, values and behavior.

TECHNICAL APPROACH

A pretest survey was administered on the first evening of the course followed by a post-test two months after the course to evaluate the effectiveness of our objectives.

Manpower: None.

Funding:	FY 76
Contractural Services	$97.50

PROGRESS

The Human Sexuality Program at Fort Sam Houston, Texas, has been presented to approximately 1800 adults over the past two years. The course critiques indicate that it has been a valuable experience to those attending.

To the question: "How informative was this course for you?" a wide variety of responses was given, ranging from very informative to not informative at all. When the question: "How informative do you feel

C-4-74 (continued)

the course was for others attending?" was asked, 75 percent replied very informative, 25 percent replied moderately informative, and none responded less than moderately informative. Of the respondents only one percent felt that the course was, or might have been, harmful to them or others, and 99 percent responded that it was at least moderately useful to those attending. 92 percent responded that a great need for the course existed, and 100 percent responded that it was appropriate to teach the course in a military setting.

Status: Completed.

Croft, H.A. Human sexuality course in the military. Mil. Med. 141:No.2, 104-108, Feb 1976.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Gallium-67 as a Scanning Agent for Malignant Neoplasms.

WORK UNIT NO.: C-141-72

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the value of Gallium-67 Citrate as a tumor localizing agent in a variety of malignant neoplasms.

TECHNICAL APPROACH

Total body images are obtained at 24, 48 and 72 hours following intravenous administration of Gallium-67-citrate in an attempt to demonstrate radionuclide localization in malignant tumors. Cleansing enemas are commonly utilized to diminish the activity due to excretion of the radiopharmaceutical in the bowel.

Manpower: None.

Funding: None.

PROGRESS

To date, 96 patients have been studied with Gallium-67-Citrate for demonstration of possible malignant neoplasms. Final anlysis of this series of patients will be obtained after completion of 100 studies. There have been no adverse reactions to the intravenous administration of Gallium-67-Citrate.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of Cisternography Utilizing ^{111}Indium DTPA.

WORK UNIT NO.: C-35-74

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the safety and efficacy of ^{111}Indium DTPA for cisternography.

TECHNICAL APPROACH

Patients are considered for this investigation project when they are referred for cisternography study by the Neurology or Neurosurgery Services. ^{111}Indium DTPA is administered intrathecally by standard lumbar puncture. Progress of the radiopharmaceutical through the subarachnoid space into the basal cisterns is monitored via whole body scan. High resolution views of the cerebral cisterns is then accomplished at varying time intervals over a 3-4 day period. When evaluating CSF rhinorrhea the nose is packed to measure radioactive leakage during the study.

Manpower: None.

Funding: None.

PROGRESS

Eighteen patients have been entered into this protocol for a variety of neurological conditions. There have been no adverse reactions to ^{111}Indium DTPA when administered by intrathecal injection. There is definite evidence that the Indium^{111} DTPA is absorbed directly across the spinal subarachnoid space since significant bladder activity is noted before the column has reached the cervical region of the spine. However, excellent imaging studies were obtained in nearly all cases and these provided useful diagnostic information to the referring clinician. Full evaluation of this series will not be performed until the series is completed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of ^{111}Indium Bleomycin (MPI Tumor Scintigraphin™).

WORK UNIT NO.: C-3-75

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., LTC, MC

ASSOCIATE INVESTIGATORS: Members of Oncology Service

OBJECTIVES

To evaluate the clinical usefulness of ^{111}Indium Bleomycin as a tumor specific radiopharmaceutical.

To demonstrate the types of neoplasms for which scintigraphy with ^{111}Indium Bleomycin has a high positive correlation with extent of disease.

TECHNICAL APPROACH

^{111}Indium Bleomycin is administered intravenously in tracer quantities to evaluate localization of this antitumor agent in a variety of malignancies. Whole body scans are performed at 24, 48 and 72 hours to evaluate areas of increased radionuclide concentration.

Manpower: None.

Funding: None.

PROGRESS

No patients are entered into this clinical investigation project since there is evidence that ^{111}Indium Bleomycin does not maintain a stable tag *in vivo*. Possibly the same results could be obtained with ^{111}Indium chloride, which is less expensive.

Status: Terminated until in vivo stability problems have been completely resolved.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Clinical Evaluation of the Thyroid by *in vivo* Radionuclidic Studies Utilizing I^{123}.

WORK UNIT NO.: C-4-75

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To substitute ^{123}I for ^{131}I in the routine evaluation of the thyroid gland. Utilizing its superior physical properties and its increased available photon yield relative to patient does, we hope to produce anatomic and physiologic data of higher overall quality and lower overall patient dose.

TECHNICAL APPROACH

Standard radioiodine uptake and scan studies utilizing probes and rectilinear scanners are to be followed.

Manpower: None.

Funding: None.

PROGRESS

Iodine^{123} has been granted new drug approval by the Food and Drug Administration and therefore is being utilized routinely in clinically applicable cases.

Status: Terminated.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: NEN Gallium-67 Citrate for Intravenous Administration.

WORK UNIT NO.: C-35-75

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: Robert L. McAuley, Jr., CPT, MSC

OBJECTIVES

To evaluate clinically the NEN brand of Gallium-67 Citrate.

TECHNICAL APPROACH

Following intravenous administration of 3 millicuries of Gallium-67-Citrate, patients are imaged at 24, 48 and 72 hours utilizing either a whole body dual probe scanner or a scintillation camera with scanning table. Cleansing enemas are given whenever possible to diminish confusing activity from bowel contaminants.

Manpower: None.

Funding: None.

PROGRESS

This entire series will be fully analyzed when 100 patients have been studied. However, a comparison of study results in a subset of 19 patients with adequate clinical follow-up for definitive diagnosis has been accomplished. In 13 patients the indications for scanning were abscesses. Two of these patients were true positives. It was possible to accurately differentiate deep abdominal abscesses from increased activity due to wound infections which were more superficial by using lateral views. In the six remaining patients, the

C-35-75 (continued)

indication was tumor. Two patients with positive studies were accurately diagnosed by Gallium scintigraphy. The four negative studies were also proven accurate.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: NEN ^{99M}Tc Stannous Glucoheptonate for Intravenous Administration.

WORK UNIT NO.: C-6-76

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: Robert L. McAuley, C

OBJECTIVES

Broad clinical evaluation of the NEN Stannous Glucoheptonate Kit after reconstitution with ^{99M}Tc-sodium pertechnetate as a diagnostic agent for studying the kidney.

TECHNICAL APPROACH

This radiopharmaceutical will be administered intravenously for evaluating renal function and structure. Scintillation camera will be used for imaging the dynamic transit of this material into and out of the renal structures. Computer analysis will be applied for obtaining time activity histogram curves and other quantitative analyses of renal function.

Manpower: None.

Funding: None.

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: MPI ^{99M}Tc-dimercaptosuccinic Acid for Intravenous Administration IND 95.

WORK UNIT NO.: C-14-76

PRINCIPAL INVESTIGATOR: Robert J. Lull, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: Robert L. McAuley, CPT, MSC

OBJECTIVES

Broad clinical evaluation (Phase III) of MPI kidney scintigraphin reagent after reconstitution with ^{99M}Tc-sodium pertechnetate as a diagnostic agent for studying the kidney.

TECHNICAL APPROACH

Up to 5 millicuries of ^{99M}Tc-dimercaptosuccinic acid will be administered intravenously for high resolution kidney imaging studies. A scintillation camer with high resolution collimator or pin-hole collimator will be utilized for optimal resolving capability. Computer analysis of the imaging data will be performed when indicated by the clinical situation.

Manpower: None.

Funding: None.

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Diastolic Augmentation Using an Intra-Aortic Balloon Pump.

WORK UNIT NO.: C-6-72

PRINCIPAL INVESTIGATOR: Robert L. Treasure, M.D., COL, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

Evaluation of an intra-aortic balloon pump providing diastolic augmentation increasing cardiac output in patients with low cardiac output due to myocardial infarction, severe cardiac disease, or following open heart surgery.

TECHNICAL APPROACH

The intra-aortic balloon is used in weening patients from cardiopulmonary bypass who are unable to generate satisfactory cardiac output. An intra-aortic balloon will be inserted in the descending aorta through a femoral arteriotomy and cardiac output increased by diastolic inflation of the aortic balloon by the AVCO pump timed by ECG.

Manpower: None.

Funding: None.

PROGRESS

Efforts to utilize the intra-aortic balloon earlier in the patient's illness are being made with some degree of success.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effects of Enflurane and Halothane on Myocardial Function in the Rhesus Monkey (Macaca Mulatta).

WORK UNIT NO.: C-2-75

PRINCIPAL INVESTIGATOR: Douglas Pritchard, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Edward D. Miller, M.D.; John R. Ritzman, M.D., MAJ, MC; Howard H. Erickson, LTC, USAF VC

OBJECTIVES

To compare the effects of two halogenated anesthetic agents on myocardial function using an invasive technique.

TECHNICAL APPROACH

Ten Rhesus monkeys were chronically instrumented with aortic flow probes, as well as left ventricular, aortic and venous pressure monitoring devices. On the morning of the experiment, the monkeys were restrained supine in a chair with which they had previously been familiarized and anesthesia was induced by mask. The animals were maintained at an initial inspired oncentration for 1 hour before recording, and at each subsequent concentration for 0.5 hour. Anesthetic levels were determined by gas-grhomatographic analysis of end-expired samples and expressed in multiple of human MAC.

Manpower: None.

Funding:	FY 76	FY 75
Consumable Supplies	$580.80	$ 18.00
MEDCASE		$5,253.58
TDY		$ 322.00

PROGRESS

Seven monkeys underwent ten separate anesthetic experiences, six with isoflurane and four with enflurane. In all cases there was a marked depression in blood pressure at increasing MAC concentrations. Blood

C-2-75 (continued)

pressure fell approximately 60% in both groups at 1 MAC and at 2 MAC blood pressure had fallen 75% from the control data. Heart rate showed a similar decline but not as marked. In agreement with depression of the peripheral signs of the cardiovascular system, dp/dt was 80% reduced at 1 MAC and almost 90% reduced at 2 MAC with both agents. The flow signal data was not recorded because of poor reproducibility.

The students' t test was applied for a two sample test and there was no statistical difference between the two groups.

Conclusions: While the present study cannot be performed on man, it points out that indirect variables may give a false impression of myocardial strength and that direct measurements of myocardial contractility give accurate information concerning the effects of any drug on the myocardium.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Prevention of Ischemic Contracture of the Left Ventricle During Aortic Cross Clamping.

WORK UNIT NO.: C-21-75

PRINCIPAL INVESTIGATOR: Robert L. Treasure, M.D., COL, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the protective effect of propanolol on the left ventricular myocardium during aortic cross clamping.

TECHNICAL APPROACH

Evaluation of left ventricular ischemic contracture and prevention of same on Propranolol was investigated using a double blind technique.

Manpower: None.

Funding:	FY 76	FY 75
Consumable Supplies	$0.00	$800.00

PROGRESS

This project has been completed and the conclusion is that Propranolol is no more effiective than hypothermia in the prevention of ischemic contracture.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Biodegradable Cuffs, an Adjunct to Peripheral Nerve Repair in Dogs.

WORK UNIT NO.: C-23-75

PRINCIPAL INVESTIGATOR: Robert L. Reid, Colonel, MC

ASSOCIATE INVESTIGATORS: Stephen C. Boone, M.D., LTC, MC; Donald H. See, M.D., LTC, MC; Duane E. Cutright, D.D., COL, DC, WRAIR

OBJECTIVES

To determine the efficacy of biodegradable cuffs at the sutured site of sectioned peripheral nerves. Specifically it will be determined if the biodegradable cuff will:

a. Prevent the in-growth of fibroblasts from surrounding tissue.
b. Maintain the regenerating axonal tissue in a parallel arrangement thereby reducing neuroma-glioma formation.

TECHNICAL APPROACH

Ten adult mongrel dogs were used in the study. The ulnar nerves in the forelimb and peroneal nerves in the hindlimbs were surgically exposed, transected, and repaired with 9-0 nylon epineural sutures using magnification. One side was repaired in the standard fashion and used as a control. The other side was repaired in the same fashion but in addition the anastomotic site was covered with a standard copolymer cuff whose cross-section diameter was 2-1/2 times that of the repaired nerve.

Nerve conduction and electromyographs were conducted on all limbs at monthly intervals and at the time of sacrifice. The electomyographer did not know which side of the animal was the test or control. After the anastomotic site was resected, light and electromicroscopic studies were performed at Walter Reed Army Institute to determine the amount of local invasiveness of scar tissue and/or reaction in the nerve to the copolymer biodegradation.

Manpower: None.

Funding:	FY 76	FY 75
Consumable Supplies	$0.00	$1,630.18

C-23-75 (continued)

PROGRESS

The animal phase of the study has been completed. The EMG study portion of the experiment was inconclusive. The light and electron microscopic studies are in progress at the Walter Reed Army Institute of Dental Research.

Status: Ongoing:

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: The Ocular Flora of the Burned Patient.

WORK UNIT NO.: C-32-75

PRINCIPAL INVESTIGATOR: Clarence G. Pramhus, M.D., MAJ, MC

ASSOCIATE INVESTIGATORS: Thomas E. Runyan, M.D., LTC, MC
Robert B. Lindberg, Ph.D.

OBJECTIVES

1. To establish the incidence of individual micro-organisms in the conjunctival flora of the acutely burned patient.

2. To see if and how these flora are altered during treatment and convalescence and particularly during changes in the lid-conjunctival-corneal anatomical relationship.

3. To compare the flora recovered from the conjunctiva with those recovered from other sources (skin, IV sites, blood, surrounding environment).

4. To study the incidence of ocular complications resulting either directly from the burn itself or from secondary changes occurring during treatment and convalescence.

5. To look at the effectiveness of various prophylactic modalities of treatment (topical Lacrilube Ophth Oint; topical or local antibiotics and/or steroids; lid, conjunctival, and/or corneal surgery; bandage soft contact lenses).

6. To assess the efficacy of various therapeutic measures once these complications have occurred (bandage soft lenses with and without antibiotics, tarsorrhaphies, conjunctival flaps, keratoplasties).

TECHNICAL APPROACH

Fifty-three patients admitted to the USAISR over a four month period were examined by one of the investigators as soon after admission as possible. Each patient was entered into one of three major groups depending on extent of burn involvement. Group I consisted of 14

patients with thermal burns who had no facial or initial ocular involvement. Group II was made up of 30 patients with facial burns who had no initial ocular involvement. Group III consisted of 9 patients who had conjunctival and corneal burns in conjunction with their facial burns. A fourth group was formed by 10 patients who developed late ocular complications. At the time of initial ophthalmological examination, a conjunctival specimen for culture and sensitivity was obtained from each eye. Biweekly conjunctival cultures were taken from each eye until the patient was transferred to the convalescent ward at which time weekly cultures were obtained. Concomitant cultures were routinely being taken by the staff of the USAISR from other sites including blood, skin, respiratory tract, urine, IV sites and surrounding environment. Ocular therapy depended on the group assignment of the patient. Patients in Group I received no ocular medication. Eight of the 30 patients in Group II were continued on neomycin-bacitracin-polymyxin B ointment four times a day. The remaining patients in this group were given either a gland ocular lubricant (Lacri-Lube^{R}) four times a day (13 patients) or no ocular medication (9 patients). Because of the corneal epithelial defects present in the patients in Group III, topical broad spectrum antibiotics were immediately instituted. The most frequently employed regimen was one in which we hourly alternated gentamycin and bacitracin ophthalmic ointments combined with ocular patching when practical.

Manpower: None.

Funding: None.

PROGRESS

A total of 525 conjunctival cultures were taken from 106 eyes of 53 patients. Staphylococci predominated with an overall recovery of S. epidermidis in 25% and S. aureus in 36% of the conjunctivae. The incidence of S. epidermidis was greatest when the face was free of thermal burn and was least when topical ocular medications were being used. This was in contradistinction to S. aureus whose incidence was markedly increased in patients who had facial burns. S. aureus was recovered most frequently (69%) from those eyes receiving the combination neomycin-bacitracin-polymyxin B. ointment.

A striking increase in the number of eyes harboring gram negative organisms and particularly Pseudomonas aeruginosa was observed in each of the groups. Three species which are rarely isolated from the conjunctiva, Enterobacter cloacae, Klebsiella pneumoniae, and Pseucomonas aeruginosa, were found in 18%, 15% and 34%, respectively. With the

exception of the development of three infected corneal ulcers in two patients with corneal burns who were harboring pseudomonas as part of their conjunctival flora, no deleterious effect on the eye was noted from the presence of these organisms. Eleven of the 15 eyes that developed superficial punctate keratitis secondary to exposure had P. aeruginosa present prior to this occurrence.

A relatively high incidence (7%) of Candida albicans was also observed, particularly in those patients receiving broad spectrum antibiotics. All three of the infected corneal ulcers subsequently yielded Candida albicans as a late isolate.

It became apparent that the flora recovered from the conjunctiva reflected what was being recovered from other parts of the body. When a conjunctival flora shift occurred, it was often possible to correlate it with a similar shift elsewhere. A retrospective analysis by phage typing for both Pseudomonas aeruginosa and S. aureus revealed that such a parallel change had indeed occurred. Strains identical with those recovered from the conjunctiva of the eye appeared concurrently in other sites.

Starting at the fifth to sixth postburn day both S. aureus and gram negative bacilli began to appear with increasing frequency. Again this reflected what was being cultured from the other tissue and fluid sites.

Summary: 106 eyes of 53 patients with severe thermal burns were studied over a four month period with serial conjunctival cultures. A dramatic shift of the normal conjunctival flora from the preponderance of S. epidermidis and corynebacterium to S. aureus and gram negative bacilli was observed. This commonly occurred on the fifth to sixth postburn day and represented colonization of the conjunctiva by bacteria recovered from other sites in the body. Despite the high incidence of Pseudomonas aeruginosa isolates (34%) of these eyes, deleterious effects were noted in only three eyes in two patients who developed infectious corneal ulcers prior to their demise.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: An Evaluation of Water Diuresis for the Prevention and Control of Recurrent Urinary Tract Infection in Women.

WORK UNIT NO.: C-34-75

PRINCIPAL INVESTIGATOR: Evelyn R. Anderson, Ph.D.

ASSOCIATE INVESTIGATOR: Mauro P. Gangai, M.D., COL, MC

OBJECTIVES

The purpose of this study is to evaluate the effect of teaching principles of fluid diuresis to females on the prevention and control of urinary tract infection.

TECHNICAL APPROACH

Each patient in the experiment was given a hydrometer and instructed in its use. Specific gravity readings were taken each morning on the first urine sample. Daily recordings were kept of their specific gravity, fluid intake, and any special remarks the patient wished to make. Both the experimental and control group were contacted monthly to inquire about their health and to insure that no complications had developed.

Manpower: None.

Funding: None.

PROGRESS

Twenty-one volunteer subjects were entered into the study. Three of the subjects moved and were dropped from the research. Nine experimental and nine control subjects were followed. The control and experimental groups completed a questionnaire and were contacted monthly by the researcher. One subject has been followed for 12 months and the data is being analyzed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Laparsocopy Under Subarachnoid Block.

WORK UNIT NO.: C-13-76

PRINCIPAL INVESTIGATOR: Robert McPherson, M.D., CPT, MC

ASSOCIATE INVESTIGATORS: Warren N. Otterson, M.D., COL, MC
Residents and Staff Dept Ob-Gyn
Residents and Staff Anesthesiology Service

OBJECTIVES

To evaluate the effectiveness of subarachnoid block as the anesthesia of choice in laparoscopy.

TECHNICAL APPROACH

Patients for elective sterilization by ligation of the fallopian tubes will be considered for this study. Patients that are immediately post-partum will not be included.

A hyperbaric subarachnoid block will be performed by residents in anesthesiology under staff supervision. After tetracaine is administered, the patient will immediately be placed in the lithotomy position and the angle of the table adjusted to obtain a pinprick level of anesthesia to the 6th thoracic livel. The patient's vital capacity, tidal volume, and minute ventilation will be measured by using a mouthpiece connected to a recording spirometer. Similar determinations will be made at 10 minute intervals during the time the abdomen is distended. Blood gas samples will be drawn at any time there is a clinical indication. An additional set of determinations will be made immediately after decompression of the abdomen.

Manpower: None.

Funding: None.

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Enflurane and Halothane on Cardiovascular Function Using Echocardiography.

WORK UNIT NO.: C-17-76

PRINCIPAL INVESTIGATOR: James E. Black, M.D., CPT, MC

ASSOCIATE INVESTIGATOR: Robert L. Watson, M.D., LTC, MC

OBJECTIVES

To assess the effects of halothane or enflurane upon the function of the cardiovascular system using a non-invasive technique.

TECHNICAL APPROACH

Twenty healthy patients scheduled for elective surgery will be studied. Patients will have echocardiograms taken 1 to 2 days prior to surgery. On the day of surgery, the patient will be brought to the operating room unpremedicated. The patient will be anesthetized with halothane or enflurane, intubated with succinylcholine and ventilation controlled to keep pCO_2 = 40 torr. Anesthetic levels will be monitored by end-tidal sampling. Echocardiograms will be taken prior to induction and at 1.0 and 1.5 MAC levels at 30 and 45 minutes after intubation.

Manpower: 1LT (5 days)

Funding:

	FY 76
MEDCASE	$1,597.75
Contractural Service	$7,246.00

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION SERVICE RESUME

TITLE: Comprehensive Rehabilitation of the Laryngectomee.

WORK UNIT NO.: C-21-76

PRINCIPAL INVESTIGATOR: Sonley R. LeMay, Jr., M.D., COL, MC

ASSOCIATE INVESTIGATORS: George A. Gates, M.D.; Edmund Lauder, M.S.; J.C. Cooper, Ph.D.

OBJECTIVES

To acquire normative data about the biological, psychological, social and employment aspects of laryngecomtee rehabilitation; to demonstrate that a comprehensive program of rehabilitation is more efficient than current methods; and to statistically validate the indices of successful and unsuccessful rehabilitation.

TECHNICAL APPROACH

When a patient is identified by his physician as requiring a laryngectomy the rehabilitative process will begin. In cooperation with the attending surgeon, the rehabilitation team will instruct the patient concerning the anatomical and physiological implications of the operation using diagrams and other prepared education materials. The patient will be visited by a successfully rehabilitated laryngectomee. A short psychological interview will be conducted involving, wherever possible, members of the family to permit the ventilation of mutual fears and anxieties. Supportive religious counseling by medically oriented ministers will be made available to the patients. The team speech therapist, surgeon and psychologist will meet with the patient's surgeon within the first postoperative week to co-ordinate a plan for individualized rehabilitation therapy.

Manpower: None.

Funding: None.

PROGRESS

Currently we have two patients enrolled in the program.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effectiveness of Haloperidol Alone and in Combination with Ephedrine as a Motion Sickness Preventative.

WORK UNIT NO.: C-32-76

PRINCIPAL INVESTIGATOR: Anton J. Jirka, M.D., LTC, MC

ASSOCIATE INVESTIGATOR: Robert L. Watson, M.D., LTC, MC

OBJECTIVES

To assess by the use of the biaxial stimulation chair, the effectiveness of haloperidol alone and in combination with ephedrine in the prevention of motion sickness.

TECHNICAL APPROACH

Ten active duty volunteer subjects assigned to Brooke Army Medical Center will be selected. Each subject's tolerance to angular acceleration in the biaxial stimulator will be measured. Approximately one week later, subjects will again be evaluated two hours after they have received, in a double blind fashion, haloperidol, haloperidol and ephedrine, ephedrine or a placebo. Each subject during the study will be tested with each one of the drugs or combinations no more frequently than once weekly. All stimulations will be produced in the biaxial chair by rotating the subjects counterclockwise at 18 rpm. Every two minutes during the rotation the subjects will be alternately tilted right and left 30 degrees from the vertical.

During the runs the subjects will be monitored by EKG, heart rate and blood pressure as well as verbal communication.

Manpower: None.

Funding: None.

PROGRESS

New protocol.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Child Advocacy Resources Expansion (CARE).

WORK UNIT NO.: C-8-76

PRINCIPAL INVESTIGATOR: Hubert A. Kelley, D.S.W., LTC, MSC

ASSOCIATE INVESTIGATORS: Michael F. Marley
Dale A. Wood, M.D., MAJ, MC

OBJECTIVES

An innovative demonstration project has been designed with the following goal: To demonstrate the effectiveness of community/Army/Air Force/ Welfare Department planning in the provision to miliary families of broad spectrum services for the prevension, diagnosis, and treatment of child abuse and neglect.

TECHNICAL APPROACH

The technical approach used to accomplish the objectives of this study is discussed under Progress.

Manpower: None.

Funding: None.

PROGRESS

Objective One; Demonstrate systematic planning of the project effort by multiple military installations, community agencies, Department of Public Welfare (DPW), and the project staff.

This objective was scheduled for the planning period and included project staffing, assessing needs and resources, gathering baseline data, and developing strategies for carrying out the project. This has been accomplished.

Objective Two: Integrate and expand a community-wide referral and resources network for maximum utilization of community and military services by troubled military families.

C-8-76 (continued)

Accomplishment of this objective, which will continue throughout the project's three years, is on schedule. CARE has received extensive publicity in the San Antonio area and an extensive local mailing list is periodically informed of the project's progress. The preliminary version of the referrals handbook is complete, and printing has begun. Plans are under way for the educational modules for civilian and military referral sources.

Objective Three: Expand existing treatment and prevention services available at Wilford Hall USAF Medical Center and Brooke Army Medical Center so that a full range of services is available to troubled military families.

The greatest amount of slippage has occurred in the accomplishment of this objective. The level of detail required in planning effective systems proved greater than anticipated. CARE's experiences in this area, however, should prove valuable to those who attempt to replicate the systems.

Objective Four: Develop and pilot-test an innovative staffing model for Texas Department of Public Welfare protective service casework for military populations.

Accomplishment of this objective is several months ahead of schedule, and the DPW Regional Administrator has agreed to assign a DPW worker to BAMC immediately. However, recent interpretations of the Federal Privacy Act have raised questions regarding the relationship of military bases and local welfare agencies. It has been decided to delay placement of a local DPW worker (to carry out mandated agency tasks as opposed to CARE workers who function as part of the military service system (until the impact of this law is clarified.

Objective Five: Perform a policy study on the Bexar County military community's response to the problem of child abuse and neglect, based on the social policy model developed by Gil.

Accomplishment of this objective has been scheduled for the second and third project years.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

APPENDIX A

SOUTHWEST ONCOLOGY GROUP PROTOCOLS

Manpower: None

Funding:	FY 76	FY 75
Contractural Service	$0.00	$1,441.80

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Combined Radiotherapy and Chemotherapy for Stages II-B, III-A and III-B Hodgkin's Disease.

WORK UNIT NO.: SWOG 160

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the safety and effectiveness with which total nodal radiotherapy could be given following MOPP chemotherapy in patients with II-B, III-A, and III-B Hodgkin's disease.

TECHNICAL APPROACH

The major criterion for study is the toxicity in the radiation portion of this protocol. The study was initially begun with three cycles of MOPP, subsequently escalated to four cycles of MOPP and after sufficient experience had been gained it was anticipated to to go six cycles.

PROGRESS

The complete response rate is 86% (121/141) for patients with final evaluations. Patients with mixed cellular Hodgkin's disease have a lower complete response rate than patients with other cellular types. Patients with clinical Stage IIIS, IIISE or clinical Stage IV have a lower response rate than those with other clinical stages.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Study of Adriamycin in Adult Acute Leukemia.

WORK UNIT NO.: SWOG 448

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of adriamycin in the remission induction of adult acute leukemia and to evolve an appropriate therapeutic regimen for this study and as a point of reference for future possible drug combinations with this agent.

TECHNICAL APPROACH

All patients registered for this study will receive adriamycin by a single IV injection. Therapy will continue according to the schedule outlined in the protocol.

PROGRESS

Complete or partial response has been noted in 23 Of 70 evaluable patients.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination and Single Drug Therapy in Breast Cancer.

WORK UNIT NO.: SWOG 450

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To determine the relative efficacy of two combination chemotherapy regimes in patients with breast cancer.

2. To determine the efficacy of single new agents in breast cancer patients who have received no prior chemotherapy.

TECHNICAL APPROACH

Patients entering the study will receive therapy on a randomized schedule as prescribed by the study protocol.

PROGRESS

The Group has a combined experience in 315 patients in four completed studies. The overall percentage of response is 40 in patients without prior chemotherapy and 30 in patients with prior chemotherapy. This protocol has been completely evaluated as far as response, survival and toxicity is concerned and a manuscript has been accepted for publication by Cancer.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Busulfan in Chronic Granulocytic Leukemia.

WORK UNIT NO.: SWOG 545/546

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate and compare intermittent and continuous remission-maintenance therapy with oral busulfan in chronic granulocytic leukemia.

TECHNICAL APPROACH

Patients with previously untreated chronic granulocytic leukemia will be allocated in random pattern and in equal numbers to one of two treatment programs for the study of remission-maintenance as prescribed in the study protocol. The initial remission-induction shall be with daily oral busulfan in the same dose for both groups as described in the study protocol.

PROGRESS

Response rate was as follows: complete, 71%; partial, 16%; mixed, 2%; none, 1%; increasing disease, 8%.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Three Combination Regimens (OAP, DOAP, COAP) for Remission-Induction and Remission-Maintenance Therapy for Adult Leukemia.

WORK UNIT NO.: SWOG 560/561

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To compare the effectiveness of three drug regimens above.

2. To estimate the effectiveness of these three regimens when cytosine arabinoside is given by 120 hour infusion.

3. To compare two maintenance regimens: intermittent remission reinduction vs. intermittent reinduction plus continuous 6MP.

TECHNICAL APPROACH

Patients meeting criterion for selection were treated as outlined in the study protocol.

PROGRESS

This study has been closed by the Southwest Oncology Group.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy for Patients with Multiple Myeloma.

WORK UNIT NO.: SWOG 734/736

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the frequency of remission induced by a four drug induction regimen (Melphalan, Prednisone, Procarbazine, Vincristine) and to compare best known maintenance with no maintenance treatment.

TECHNICAL APPROACH

Patients meeting selection criteria were treated as outlined in the study protocol.

PROGRESS

This study has been closed by the Southwest Oncology Group.

STATUS: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Hodgkin's Disease: Remission Induction with MOPP + Bleomycin

WORK UNIT NO.: SWOG 774/775

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine the comparative effectiveness of MOPP alone and in combination with two different dose schedules of bleomycin for complete remission and induction in patients with disseminated Hodgkin's disease.

2. To determine the relative effectiveness of MOPP and radiation therapy followed by MOPP and intensive MOPP in remission consolidation in those patients achieving complete remission.

TECHNICAL APPROACH

Patients meeting selection criteria were treated as outlined in the study protocol.

PROGRESS

The final updates analysis of the MOPP #4 study has been completed. This study has been closed for 8 months and all of the patients on the remission induction limb of the study have completed their treatment.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Cyclophosphamide, Vincristine, Prednisone and Bleomycin for Non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWOG 780

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the side effects and toxicity of a combination of bleomycin with cyclophosphamide. vincristine, and prednisone (COP) in patients with disseminated non-Hodgkin's malignant lymphoma.

TECHNICAL APPROACH

Approximately 80 evaluable patients in each of the two major malignant lymphoma categories - lymphosarcoma and reticulum cell sarcoma - should be sufficient for the study. Dosage and treatment will conform to the schedule outlined in the study protocol.

PROGRESS

The Southwest Oncology Group has completed this study. A manuscript is being prepared for submission for publication in Cancer.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Radiotherapy-Chemotherapy (MOPP) for Stages I and II A and B Hodgkins.

WORK UNIT NO.: SWOG 781

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare total nodal radiotherapy and involved field radiotherapy plus MOPP chemotherapy in patients with Stages I and II, A and B Hodgkin's disease.

TECHNICAL APPROACH

At the time of registration of the patient, randomization to one or two treatment programs will be made: (1) total nodal radiation, or (2) involved field radiation followed by MOPP chemotherapy. Therapy will be administered according to the schedule outlined in the study protocol.

PROGRESS

The complete response rates for final evaluated patients are: total nodal 96% and involved field + MOPP 92% ($P>.13$). There is evidence of different complete response rate by symptoms ($P<.03$) and patholgoical stage ($P<.03$). The male response rate has increased and there is now no difference due to sex. There is a suggested difference in response rate by age ($.05<P<.10$). Involved field + MOPP group has more frequent severe or life-threatening toxicity (25%) than the total nodal (2%). There have been no fatalities due to toxicity.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: POMP Combination Chemotherapy of Adult Acute Leukemia

WORK UNIT NO.: SWOG 920

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the frequency of remission induction in adult acute leukemia.

TECHNICAL APPROACH

Adults with acute leukemia who remain in continuous complete remission following initial induction therapy will be eligible for three courses of POMP therapy as late intensification. The procedures outlined in the addendum to the protocol should be followed for patients to be entered on Late Intensification therapy.

PROGRESS

Since receipt of the addenum, no new patients have been added.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Methyl CCNU for the Treatment of Various Solid Tumors Except Carcinoma of the Breast.

WORK UNIT NO.: SWOG 7200

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the effectiveness of intermittent oral methyl CCNU in the treatment of various solid tumors.

TECHNICAL APPROACH

This study remains open for Hodgkin's disease only. Therapy will conform to the schema outlined in the study protocol.

PROGRESS

This study has been closed by Southwest Oncology Group.

Status: Completed.

Tranum, B.L., Gottlieb, J.A., Haut, A., Rivkin, S. and Weber, E.: Methyl CCNU in Treatment of Solid Tumors and Lymphomas. Cancer 35:1148-1153, 1975.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: CHOP vs HOP Combination Chemotherapy for Remission Induction and COP vs OAP Combination Chemotherapy for Maintenance in non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWOG 7204/7205

PRINCIPAL INVESTIGATOR: Robert P.Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To compare the remission inducing effectiveness of the 4-drug regimen--Cytoxan, hydroxyldaunomycin (adriamycin), oncovin, and prednisone...CHOP -- to the 3-drug regimen -- hydroxyldaunomycin, oncovin, prednisone...HOP -- given by similar schedules.

2. To compare two maintenance arms after complete remission induction and remission consolidation. One arm will utilize cyclophosphamide, vincristine and prednisone (COP) and the other arm, cytosine arabinoside, vincristine and prednisone (OAP).

TECHNICAL APPROACH

Approximately 100 valid patients on each major induction limb should permit successful evaluation of this protocol. Courses of therapy will be instituted at two week intervals. Dosage modifications will be made for subsequent courses depending on the patient's response. Dosage and treatment intervals will be in accordance with the schedule outlined in the study protocol.

PROGRESS

Study completed and accepted for publication by Cancer. The final figures show complete response rate on CHOP of 59% and 51% on the HOP limb. Patients with Stage III disease had higher response rates as did those with nodular disease.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: 5-Azacytidine in Patients with Acute Leukemia.

WORK UNIT NO.: SWOG 7209

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the effectiveness of 5-Azacytidine in the treatment of acute leukemia.

TECHNICAL APPROACH

A minimum of 14 evaluable patients in each of the major diagnostic groups (acute lymphocytic leukemia and acute myelocytic leukemia) will be entered into the study. Remission induction and remission maintenance dosages will be administered according to the schema outlined in the study protocol.

PROGRESS

One hundred patients were registered on this study. Eighty-eight were evaluable with 13 complete responses, 14 partial responses, 12 failures and 3 hematologic improvements. The study has been closed by the Southwest Oncology Group.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Comparison of Two Combination Chemotherapy Programs in the Treatment of Disseminated Malignant Melanoma.

WORK UNIT NO.: SWOG 7216

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To compare two slightly different combination programs - DIC, BCNU and Hydrea versus DIC, VCR, BCNU and Hydrea - on the frequency, magnitude, duration of tumor regression and survival in patients with disseminated malignant melanoma.

TECHNICAL APPROACH

Approximately 75 patients will be entered into the study. Dosage and treatment will conform with the schema outlined in the study protocol.

PROGRESS

Although this study was closed, continued submission of flow sheets for survival was encouraged. An update of this study through February 1975 together with the entire Southwest Group experience with DTIC in melanoma was presented at a recent new drug seminar at the NIC. This will be published in Cancer Chemotherapy Reports.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Evaluation of Colorectal Carcinoma Comparing Bolus Weekly 5-FU vs. the Combination of Methyl CCNU plus Bolus Weekly 5-FU.

WORK UNIT NO.: SWOG 7302

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To estimate the effectiveness of the combination therapy and 5-FU alone.

2. To determine whether the objective remission rate of the combination therapy is significantly superior to that of 5-FU alone.

TECHNICAL APPROACH

All patients prior to receiving the drugs will be randomized between the two arms of the study. The randomization will be designed so that three patients will receive 5-FU plus MeCCNU for every patient on 5-FU. Patients will be stratified into two groups: Patients with liver metastases only; patients in all other categories combined (including those with liver metastases plus metastases to other sites). Therapy will conform with the schema outlined in the study protocol.

PROGRESS

This study has been closed by the Southwest Oncology Group in October 1974. No new patients have been entered at Brooke Army Medical Center.

Status: Completed.

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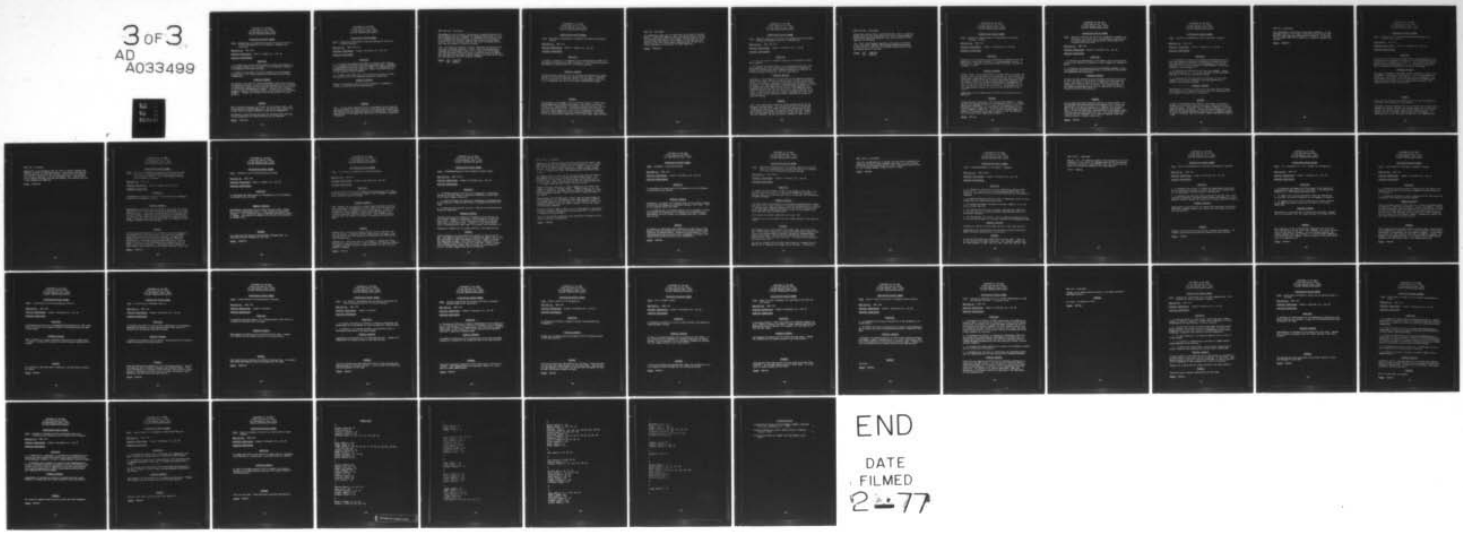

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DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy of Disseminated Testicular Carcinoma with Vinblastine and Bleomycin or Actinomycin-D, Bleomycin and Vincristine.

WORK UNIT NO.: SWOG 7303

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To compare the relative effectiveness of velban and bleomycin vs. vincristine, bleomycin and actinomycin-D in the remission induction of disseminated testicular carcinoma.

2. Attempt at recruitment of partial responses into the complete response pool via a crossover mechanism involving the above agents (reinduction).

TECHNICAL APPROACH

All patients with stage III (supradiaphragmatic) metastatic testicular carcinoma are eligible to enter the study regardless of prior radiation or chemotherapy, except for those patients who have had a trial of one of the selected chemotherapeutic agents. Patients will be randomly assigned to receive vinblastine/bleomycin or actinomycin-D/vincristine/bleomycin. Therapy will conform to the outline given in the study protocol.

PROGRESS

With 47 patients analyzed, the CR rate for the VLB/Bleo limb is 63% versus 30% for the ACT/VCR/Bleo limb. The latter limb resulted only in skin toxicity, whereas VLB/Bleo saw mainly myelosuppression.

The protocol, which has been held open for the most active arm (Vinblastine-Bleomycin) was closed officially by the Committee.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy of Multiple Myeloma in Previously Untreated Patients.

WORK UNIT NO.: SWOG 7305-7306

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To evaluate the frequency and degree of response from treatment with a melphalan-adriamycin-prednisone combination (MAP), a melphalan-cyclophosphamide-prednisone combination (MCP), and a melphalan-cyclophosphamide-BCNU-prednisone combination (MCBP) in patients with previously untreated myltiple myeloma.

2. To compare the results with recent historical controls of about 500 patients treated with melphalan-prednisone combinations.

TECHNICAL APPROACH

Patients entering the study will receive therapy on a randomized schedule as prescribed by the study protocol.

PROGRESS

7305 - For six month treatment trials, the response rate of about 40% for each treatment is almost identical to that resulting from previous SWOG studies with other melphalan-prednisone combinations. The response rate with MCP is the highest but there are no statistically significant differences.

SWOG 7305-7306 (continued)

The ambiguity in this protocol concerning the required duration of induction before they are considered for remission maintenance or crossover treatment has been discussed. An amendment to this protocol will be distributed that requires randomization on remission maintenance protocol 7313 or on crossover protocol 7306 after six months (but no more than nine months) of induction therapy.

7306 - This protocol evaluates crossover treatments for patients with less than a 75% tumor reduction. So far, only a few patients have responded and the frequency (about 15%) is similar to the incidence that one would expect from slow onsets of remission after six months. Only rare patients have shown a marked change in the slope of the curve for tumor mass plot with the crossover treatment.

Status: 7305 - Completed.
7306 - Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Maintenance Chemotherapy of Responsive Patients with Multiple Myeloma.

WORK UNIT NO.: SWOG 7313

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To compare a combination of mephalan-cytoxan-BCNU-prednisone (MCBP) with azathioprine-prednisone plus MCBP reinduction in the long term remission maintenance of response patients with multiple myeloma.

TECHNICAL APPROACH

Eligible responsive patients will be registered and maintenance randomization will be by each induction regimen (MAP, MCP, MCBP). Treatment will be as outlined in the study protocol. Approximately 30 patients will be randomized into each of the remission maintenance groups.

PROGRESS

This protocol, which compares the consolidation effects of MCBP versus imuran-prednisone with MCBP reinforcement, was closed to new entry 11 June 1975. Approximately 40 responsive patients have been enrolled into each limb of this study. The remission duration and survival curves for these appear to be better than a recent group of comparable patients treated indefinitely with melphalan-prednisone. This trend is not yet statistically significant, but if the current trend continues

SWOG 7313 (continued)

this difference likely will be significant by the time of the next review. A sufficient number of cases have been entered to achieve the scientific objectives of the program. Kinetic analysis of this protocol shows that neither arm is superior to the other and the addition of the cycle active agent combination has not made an apparent difference in the kinetics of tumor regression.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Remission-Induction for Adult Acute Leukemia with Ten-Day OAP; Remission-Maintenance with OAP vs. OAP plus BCG.

WORK UNIT NO.: SWOG 7315/7316

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To test the remission induction efficacy of ten-day OAP in adult acute leukemia.

2. To compare the effectiveness of 5-day maintenance OAP with 5-day maintenance OAP plus BCG in prolonging the duration of complete remission of patients achieving a complete remission on 10-day OAP induction which was followed by 5-day OAP consolidation.

TECHNICAL APPROACH

A minimum of 135 patients will be entered into the remission-induction phase of the study. OAP will be administered x 10 days as prescribed by the study protocol. Bone marrow aspirations will be done on day 14 and every 4 or 5 days thereafter to determine when the marrow is cleared of leukemic cells and when recovery from the marrow hypoplasia has occurred sufficient to start the next course. Following the second induction course of OAP, the bone marrow will again be allowed to recover. If the patient achieves a complete remission after the second course of OAP, he will then receive three consolidation courses of 5-day OAP therapy.

PROGRESS

7315 - This protocol was closed for further patient entries by the Southwest Oncology Group. The conclusion was that the ten-day OAP is better than any prior remission induction therapy that has been investigated by the Group. The complete response rate for ten-day OAP is better than that for five-day OAP at the .05 level. Correction for prognostic factors will gives a probability that this is

SWOG 7315/7316 (continued)

better than five-day OAP by approximately 90%. This is a very important study for the Group since it is the first non-randomized historically controlled Groupwide study, and it provides a very important new technique.

7316 - This is an extremely important study since it forms the pattern for future combined immunotherapy-chemotherapy studies. At this time it is too early to calculate survival rates in the maintenance phase of the study.

Status: 7315 - Completed.
7316 - Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Immunotherapy and Chemotherapy in Localized Osteogenic Sarcoma.

WORK UNIT NO.: SWOG 7317

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

Evaluation of the efficacy of the combination of transfer factor and combination chemotherapy (COMPADRI II-Cyclophosphamide, Oncovin, Methotrexate, Melphalan and Adriamycin SWOG 7317 study) in localized osteogenic sarcoma.

TECHNICAL APPROACH

Transfer factor will be administered in dosage levels of two units per day for a total of eight units to be given prior to the initiation of chemotherapy completing the administration 48 hours prior to treatment. Thereafter, during the 250 day outlined chemotherapy treatment plan, the transfer factor will be given during lapses in chemotherapy, 14 days from day one of the pulses of therapy and in the amount of two units per day for 2 days or four units total. The patients will receive approximately 40 units by the end of the prescribed 350 day course.

Chemotherapy will be administered according to the protocol plan in SWOG 7317.

PROGRESS

Interim analysis of the early cases treated with Compadri II regimen has shown an alarming frequency of late metastases (16, 19, 19 and 26 months after amputation). It is noted that the cumulative dose of adriamycin in this study was considerably below the cumulative dose used in Compadri-I (SWOG 979). It was decided to amend Compadri II schedule by increasing the adriamycin pulses so that the cumulative dose would more closely approximate Compadri I.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Remission-Induction for Adult Acute Lymphocytic Leukemia with Adriamycin, Vincristine and Prednisone Remission-Maintenance with Methotrexate and 6-Mercaptopurine Reinforcement with Prednisone and Vincristine.

WORK UNIT NO.: SWOG 7401

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To evaluate the effectiveness of Adriamycin, Vincristine and Prednisone in the induction of remission in acute lymphocytic leukemia in adults.

2. To evaluate the following remission maintenance program: daily 6-mercaptopurine and weekly methotrexate, plus periodic reinforcement with prednisone and vincristine.

TECHNICAL APPROACH

Patients who have received no prior adriamycin and who have ALL with at least 30% blasts in the marrow are eligible for entry into the study. Only adults 15 years of age or older will be studied. Approximately 37 patients will be entered. The remission-induction and remission-maintenance phases will be administered according to instructions in the study protocol.

PROGRESS

To date there have been 34 patients entered, 32 are evaluable. Of the previously untreated patients with adequate trials, there have been 18 CRs, 1 PR and 1 patient with no response for a CR rate of 69% of the total patients and 90% of the patients with adequate tiral. Of the five previously treated patients with adequate trials, there has been one early death and 3 CRs. All 10 AML patients had received previous treatment; all 10 received adequate tirals and 2 CRs are noted, 1 CR was a blastic CGL.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy Study of Metastatic Sarcomas.

WORK UNIT NO.: SWOG 7402

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To determine the efficacy of combination chemotherapy with two four-drug regimens in patients with metastatic sarcoma. The four-drug combinations are CY-VA-DIC (cyclophosphamide, vincristine, adriamycin and DIC) and CY-VA-DACT (cyclophosphamide, vincristine, adriamycin, and actinomycin D).

2. To determine the efficacy of two cross-over regimens - methyl CCNU and actinomycin D - for patients failing CY-VA-DIC and methyl CCNU and DIC for patients failing CY-VA-DACT.

3. To determine tho survival pattern of patients on this study compared with previous adriamycin-containing combinations in patients with metastatic sarcoma.

TECHNICAL APPROACH

Approximately 75 patients on each of the four-drug induction limbs will be evaluated. Dosage and treatment will be in accordance with the schedule outlined in the study protocol.

PROGRESS

A total of 577 patients were entered in this study. Of the 283 patients on the CY-VA-DIC arm, 207 are fully evaluable and 24 partially evaluable. There have been 27 complete responses, 70 partial responses and 48 no responses. Complete and partial/eligible = 39%. The CY-VA-DAC arm had 294 patients entered with 22 complete responses, 54 partial responses, and 68 no change. Complete and partial/eligible = 29%.

SWOG 7403 (continued)

This constitutes a statistically significant difference. In the crossover portion of the study, 54 patients received methyl CCNU and DTIC; there were only three partical responses. 53 patients received methyl CCNU and actinomycin-D; no partial responses were observed.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adriamycin, 5-FU, Cyclophosphamide and Methotrexate for Advanced Breast Cancer.

WORK UNIT NO.: SWOG 7405

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To test three different drug combinations utilizing adriamycin as the base drug in the treatment of patient with breast cancer who have received no prior chemotherapy in order to: (1) determine the relative efficacy of adding drugs singularly or in combination to adriamycin and (2) determine the comparative toxicity of the regimens.

TECHNICAL APPROACH

This study is designed to determine whether adriamycin + 5-FU + cyclophosphamide + methotrexate or adriamycin + 5-FU + cycophosphamide results in a significantly high response rate than adriamycin + 5-FU. Approximately 76 patients will be entered into each treatment group. Each of the above regimens will be administered according to the schedule outlined in the study protocol.

PROGRESS

A total of 327 patients were entered before the study was amended in July 1975. 95% of these are now evaluable.

The overall complete response rate for all patients was 11% and that of complete plus partial was 45%. The response rates for the three arms are 41%, 44% and 49%, respectively, for the addition of 5-FU, 5-FU + Cytoxan, and 5-FU + Cytoxan + Methotrexate to the Adriamycin. In comparing these results with those of SWOG 450, it is apparent that

SWOG 7405 (continued)

adding 5-FU to the adriamycin does not lead to a better response rate than that achieved with adriamycin alone. This becomes even more significant when one considers the remission duration with this combination, which is identical to that of adriamycin alone. None of these results compare favorably with the 59% response rate obtained with the 5-drug combination of SWOG 450.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: VP 16-213 (4^1-Dimethyl-Epipodophyllotoxin-B-D-Ethylidene Glucoside) by Intravenous Infusion on Five Consecutive Days Every Three Weeks in Adults with Hodgkin's Disease and Non-Hodgkin's Lymphomas.

WORK UNIT NO.: SWOG 7407

PRINCIPAL INVESTIGATOR: Robert P. Bøwman, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the efficacy of VP-16 in adult patients with Hodgkin's disease and non-Hodgkin's lymphoma.

TECHNICAL APPROACH

Approximately 24 patients will be studied in each group. The initial dose of VP 16-213 will be administered by IV infusion daily for five consecutive days. Courses will be administered at three week intervals as tolerated. Subsequent courses should not be repeated until the nadir of blood counts has been reached and the counts are recovering. Subsequent doses will be administered in accordance with the schedule outlined in the study protocol.

PROGRESS

Of the 50 registered patients, 45 (16 Hodkin's and 29 non-Hodgkin's) were eligible and of the 25 evaluable and 13 partially evaluable cases, there have been three partial responses. Of eight cases evaluable for toxicity at the revised dose schedule, there are three severe or life-thratening myelosuppression cases. They are unable to account for the astonishingly low response rate as compared to that of the literature. The extensive prior therapy of these patients may account for the difference, but that is not clear.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chromomycin A_3 for Advanced Breast Carcinoma.

WORK UNIT NO.: SWOG 7408

PRINCIPAL INVESTIGATOR: Robert P. Bowman, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To investigate the effectiveness of Chromomycin A_3 in the treatment of advanced breast carcinoma.

TECHNICAL APPROACH

Approximately 25 patients will be entered into the study. Chromomycin will be administered daily x 5 days through an established running IV. Five consecutive days of treatment constitute at course of therapy. Two courses of treatment with toxicity will constitute an adequate trial.

PROGRESS

This study has been closed by the Southwest Oncology Group. No reportable data are available at this time.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum in Lymphomas and Multiple Myeloma.

WORK UNIT NO.: SWOG 7413

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the activity of cis-diamminedichloroplatinum II NSC-119875, (CACP) in patients with refractory Hodgkin's and non-Hodgkin's lymphoma and in refractory multiple myeloma.

TECHNICAL APPROACH

CACP, 75 mg/M^2, will be given as a single rapid intravenous injection every three weeks. An adequate trial will consist of two courses and all patients will be followed for the six week period. If there is evidence of a tumor response or stable disease the drug may be continued at three week intervals indefinitely. With evidence of progression after two courses of the agent, the patient will go off the study.

PROGRESS

Myeloma Group - Of the five patients entered in this study thus far, only one patient is evaluable and had stabilization of disease. Significant toxicity has been observed including nausea and vomiting and renal insufficiency.

Lymphoma Grou - There have been six non-Hodgkin's lympoma and 4 Hodgkin's disease patients entered. There have been 1 of 4 partial responses in Hodgkin's disease and only one improved patient of the 6 with non-Hodgkin's lymphoma.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemoimmunotherapy of Acute Leukemia in Adults (CIAL).

WORK UNIT NO.: SWOG 7416/17

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To determine whether with the use of sequential or simultaneous adriamycin and ARA-C there is significant difference in their ability to induce complete remission.

2. To study the effects of combination chemotherapy and immunotherapy on the duration of remission and survival in patients with acute leukemia.

3. To identify those patients with ALL vs AML who are vincristine and prednisone responsive.

TECHNICAL APPROACH

Patients fulfilling the criteria for treatment will be divided into two different categories, depending on their peripheral circulating blast count. Category 1 is for those patients with a circulating blast count of less than 30,000. Category 2 is for those patients with a circulating blast count equal to or greater than 30,000/cu. ml.

Therapy will conform with the schema outlined in the study protocol.

PROGRESS

Overall prognosis for CIAL patients was superior to that for 10-day OAP. The complete remission rate was significantly higher, 58% vs. 53%, when adjustment was made for prognostic factors. Length of response was significantly longer, 75% of patients being in remission at 30 weeks compared with 60% at 30 weeks for 10-day OAP. Finally survival was also significantly longer, 62% of patients on CIAL being still alive at 40 weeks compared with 48% for 10-day OAP.

SWOG 7416/17 (continued)

Prognosis of the patients did not differ by initial blast count. Complete remission rate for patients with <30,000 blasts was 57% compared with 61% for patients with ≥30,000 blasts. Lengths of remission and survival curves did not differ significantly between groups, though there was a higher early death rate among patients with 30,000 blasts or more.

The response rate to initial VP was 24% for patients under 60 years of age compared with 13% in 13 patients 60 years of age or more. The response rate to VP-Ad-ARA-C in older patients was 35% while that to Ad-OAP was 45%. Hence, response rate was poor for older patients and was not higher among patients treated initially with VP.

Among VP failures, there was no overall superiority for either simultaneous or sequential adriamycin-ARA-C. Complete remission rate was higher for sequential treatment; however, length of response was longer for simultaneous treatment. Overall survival was nearly the same in both groups.

Among patients with 30,000 blasts or more, there was some evidence of oerall superiority for simultaneous rather than sequential treatment. The complete remission rate was higher for simultaneous treatment, the lengths of remission were very similar; however, survival was longer on simultaneous treatment.

Patients achieving complete remission on VP alone appear to have poorer subsequent prognosis than patients achieving remission on simultaneous or sequential adriamycin-ARA-C.

The only statistically significant fact predictive of response in this study was the age of the patient.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234

INVESTIGATION PROJECT RESUME

TITLE: Chromomycin in Multiple Myeloma.

WORK UNIT NO.: SWOG 7423

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To investigate the effectiveness of Chromomycin A_3 in the treatment of advanced multiple myeloma.

TECHNICAL APPROACH

Chromomycin, 0.75 mg/M^2, will be given daily as 10-20 minute infusion in 50-100 ml D5W through an established running IV for 5 days. This will be repeated every three weeks.

It is estimated that 14 evaluable patients will be adequate to determine whether 20% response will be expected at 5% rejection error. Approximately 25 will estimate this response rate with a standard error of $\pm$8%.

PROGRESS

No evidence of significant tumor regression has been noted in four patients receiving chromomycin and two other patients showed slight reductions of myeloma protein. Nephrotoxicity developed in 4 of 9 treated patients and the protocol will be amended to include a dose reduction for patients with any renal insufficiency.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston Texas, 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy Utilizing BCNU, Hydroxyurea and DTIC (BHD) with and without BCG, and DTIC with BCG in the Treatment of Patients with Disseminated Malignant Melanoma.

WORK UNIT NO.: SWOG 7424-25

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To compare the effectiveness of BHD (3-drug regimen) alone, BHD in combination with BCG, and DTIC in combination with BCG for remission induction, duration of remission and survival in patients with disseminated malignant melanoma.

TECHNICAL APPROACH

Since BCNU, DTIC and Hydroxyurea are principally myelosupressive, dosage and time intervals were calculated to avoid the maximum toxicity occurring at the same time. Separate randomizations are set up for patients with normal and impaired bone marrow reserve, as well as for patients with brain metastases and liver metastases.

Total number of patients needed for this study: 188.

Treatment will be in accordance with the schema outlined in the study protocol.

PROGRESS

The response rate is 26% for BHD, 28% for BHD + BCG, and 20% for DTIC + BCG. Statistically, there was no difference between these response rates. Toxicity was primarily mild to moderate leukopenia, thrombocytopenia, nausea and vomiting. Thirteen patients had mild BCG reaction in the form of fever, chills and local reactions. No evidence of disseminated BCG disease was noted.

The time to response did not differ significantly by treatment and the median time to response was 38 weeks for all patients. The survival

SWOG 7424/25 (continued)

curve for the BHD patients is poorest over the first 24 weeks but the curves are similar for each treatment and there is no real evidence of statistical difference among the curves. The median survival time for all treatment groups is approximately 24 weeks.

Status: *Ongoing.*

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemoimmunotherapy in Non-Hodgkin's Lymphoma.

WORK UNIT NO.: SWOG 7426/27

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To compare the effectiveness of two chemotherapy regimens (CHOP + Bleomycin; COP + Bleomycin) or chemoimmunotherapy (CHOP + BCG) for remission, induction in previously untreated patients with non-Hodgkin's lymphomas.

2. To establish baseline and serial data on immunologic status in both chemotherapy and chemoimmunotherapy groups.

3. To evaluate systematic restaging of patients judged to be in complete clinical remission.

4. For patients proven to be in complete remission after induction, to test the value of continued maintenance immunotherapy (BCG) vs no maintenance treatment.

5. For patients who only achieve a partial remission during induction, to test the effectiveness of continued treatment with chemoimmunotherapy.

TECHNICAL APPROACH

Therapy will conform with the schema outlined in the study protocol.

Approximately 150 valid patients on each major induction limb should permit successful evaluations of this protocol.

PROGRESS

A total of 321 patients have been entered on this study. There are now 121 patients with final evaluations. The complete response rate for these patients is CHOP + BCG 57%, CHOP + Bleo 53%, and COP + Bleo

SWOG 7426/27 (continued)

60% (P = .78). The complete response rates for patients w-th final evaluation is 57%, and is not different from the 55% for patients with final evaluation on the CHOP-HOP study. The response rate appears to be increasing somewhat as the study matures.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Methyl CCNU-Adriamycin for Patients with Metastatic Sarcomas.

WORK UNIT NO.: SWOG 7431

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To determine the efficacy of combination chemotherapy using Methyl CCNU for metastatic sarcomas in patients who have prior refractoriness for cyclophosphamide vincriseine and/or Actinomycin D.

2. To determine the remission duration pattern of patients under study comparing intermittent continuous administration of Adriamycin in those patients initially induced into remission with Methyl CCNU and Adriamycin.

TECHNICAL APPROACH

Approximately 80 patients will be studied over a period of 18-24 months. Dosage and treatment schedule will conform with the schema outlined in the study protocol.

PROGRESS

Thusfar, there have been eleven patients evaluable for response. One complete response and three partial responses have been observed.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: 5-FU + Mitomycin-C vs. 5-FU + MeCCNU in GI Malignancies.

WORK UNIT NO.: SWOG 7434

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To determine and compare the effectiveness of two combination chemotherapies in gastrointestinal carcinomas: 5-FU infusion and Mitomycin C vs. 5-FU infusion and Methyl CCNU.

2. To compare the toxicities produced by these two combinations to allow the decision as to which of the two regimens is superior.

3. To compare the results of this study with the results observed in the SWOG 7302 protocol, which was 5-FU bolus vs 5-FU bolus + Methyl CCNU.

TECHNICAL APPROACH

Approximately 176 patients will be entered into the study. Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

This study has a total of 235 patients registered with 119 on the 5-FU + Mitomycin-C arm and 116 on 5-FU + MeCCNU. Most of the patients are still too early to evaluate. For the evaluable patients, the overall response with 5-FU + Mitomycin C is 20.8% (10/48) compared to 8.5% (4/57) for 5-FU + MeCCNU. Also of interest in this early evaluation is the myelotoxicity.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Piperazinedione in Malignant Lymphoma or Myeloma.

WORK UNIT NO.: SWOG 7435

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To establish the objective tumor response rates, both partial and complete, for patients with refractory lymphomas, and the duration of such responses.

2. To establish the objective tumor response rates and their durations in patients with refractory multiple myeloma.

TECHNICAL APPROACH

Since the primary purpose of the study is to estimate the effectiveness of Piperazine in patients with Hodgkin's disease, non-Hodgkin's lympoma, and multiple myeloma, sufficient patients will be entered into the study to obtain reasonably precise estimates of the complete and partial remission rates. Thus the study will proceed until at least 24 patients have been studied in each disease category. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

Thirty eight patients have been entered into this study. Objective partial responses were observed in 3 of 5 evaluable patients with Hodgkin's disease and 2 of 5 patients with non-Hodgkin's lympoma. An improvement was noted in two other patients, both with non-Hodgkin's lymphoma. No response of any degree occurred in 12 patients with resistant myeloma. Therefore the study remains open to the lymphoma group only.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cis-platinum for Gu-Gyn Malignancies, Phase II.

WORK UNIT NO.: SWOG 7438

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the activity of cis-diamminedichloroplatinum (II) (NSC 119875, CACP) in patients with malignant diseases of the genitourinary and gynecologic organs.

TECHNICAL APPROACH

CACP, 75 mg/M^2, as a single intravenous injection will be administered q 3 weeks. A minimum of 15 patients in each histologic subtype will be studied.

PROGRESS

In 35 patients, there have been 7 responses, 5 of which were in testicular tumors.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Cyclocytidine in Melanoma, Phase II.

WORK UNIT NO.: SWOG 7504

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the effect of cyclocytidine chemotherapy on the frequency, magnitude and duration of tumor regression and on the survival of patients with disseminated malignant melanoma.

TECHNICAL APPROACH

A minimum of 25 patients will be studied. Cyclocytidine will be administered as outlined in the study protocol.

PROGRESS

There has been partial response in 1 of 10 evaluable patients. Toxicity was primarily mild to moderate leukopenia and thrombocytopenia. Orthostatic hypotension was reported in three patients, and jaw pain in seven patients. The study will remain open as a second line protocol until appropriate patient accrual has been obtained.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Piperazinedione for Advanced Breast Carcinoma.

WORK UNIT NO.: SWOG 7508

PRINCIPAL INVESTIGATOR: Joseph D. McCracken

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the effectiveness of 2,5-Piperazinedione (NSC 135758) in treatment of advanced breast carcinoma.

TECHNICAL APPROACH

Approximately 34 patients will be entered into the study. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

This study has been closed by the Southwest Oncology Group. No patients from Brooke Army Medical Center were entered into the study.

Status: Completed.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: 5-FU, MeCCNU + Radiotherapy with or without Testolactone for Localized Adenocarcinoma of the Exocrine Pancreas.

WORK UNIT NO.: SWOG 7509

PRINCIPAL INVESTIGATOR: Joseph D. McCracken

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To evaluate the effect on survival of intensive radiotherapy and chemotherapy (5-FU and MeCCNU) of localized pancreatic adenocarcinoma.

2. To evaluate, in a randomized manner, any beneficial effect of testolactone when added to the above regimen.

TECHNICAL APPROACH

Approximately 100 patients will be registered per year. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

Only four patients have been registered, which is far below the anticipated acrual of 100 cases per year. It is too early to evaluate the four participants in this study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Adjuvant Chemotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel.

WORK UNIT NO.: SWOG 7510

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU and 5-Fluorouracil and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Guerin (BCG) on the disease-free interval and survival of patients with Duce C large bowel adenocarcinoma.

TECHNICAL APPROACH

A minimum of 52 patients will be entered into each of the two groups. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

There are 16 patients registered on this study with 11 too early to evaluate. Both regimens seem to be tolerable, however, it is too early to assess effectiveness.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Baker's Antifol in GI Malignancies.

WORK UNIT NO.: SWOG 7512

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the efficacy of Baker's Antifol in gastrointestinal malignancies.

TECHNICAL APPROACH

Therapy will be administered in accordance with the schema outlined in the study protocol.

PROGRESS

Fifty-six patients have been entered into the study. There have been two failures, one stable disease, and one early death. The protocol has been amended to treat good risk patients with 250 mg/M^2; the dose for bad risk patients remains the same.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: VP-16 in Breast Cancer.

WORK UNIT NO.: SWOG 7514

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the efficacy of VP-16 in adult patients with metastatic adenocarcinoma of breast.

TECHNICAL APPROACH

At least 14 evaluable patients will be entered into this study. If one or more positive responses are obtained, then entry of further patients into the protocol will be considered. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

A total of 9 patients have entered this study, one of whom had a partial response, three no change and five increasing disease.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase III Study of Squamous Cell Carcinoma of the Head and Neck Region.

WORK UNIT NO.: SWOG 7519

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine whether a three drug combination treatment program will give a superior response rate and/or a longer remission duration than methotrexate alone in patients with squamous cell carcinoma of the head and neck region.

TECHNICAL APPROACH

Approximately 60 patients will be entered into the study. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

Seven patients have been entered into this study with three being evaluable. Two of these three resulted in early death. It is too early to assess response on this study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Phase II Study of Galactitol in Advanced Cancer Patients.

WORK UNIT NO.: SWOG 7520

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To determine the efficacy of Galactitol in the treatment of advanced cancer.

2. To observe for factors predisposing to excessive myelosuppression and for other toxicities not observed during Phase I studies of this drug.

TECHNICAL APPROACH

A minimum of 14 evaluable patients in each disease committee category are needed to permit a determination of at least a 20% efficacy rate with a 95% likelihood of not missing an effective agent. Therapy will be in accordance with the schema outlined in the study protocol.

PROGRESS

New study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Combination Chemotherapy with or without Immunotherapy in High Risk Melanoma Patients: An Adjuvant Study.

WORK UNIT NO.: SWOG 7521

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

1. To determine the efficacy of BCNU, hydroxyurea, and imidazole carboxamide (BHD) in preventing the recurrence of disease and prolonging the survival of patients with primary malignant melanoma who have received definitive surgical treatment for their primary lesions, have no evidence of residual disease but in whom by the clinical and pathological characteristics of the primary lesion can be predicted to have a high incidence of recurrence.

2. To determine the efficacy of combination chemotherapy (BHD) with and without BCG in preventing the development of metastases and prolonging the disease-free interval and survival of patients with recurrent malignant melanoma which has been surgically excised ("minimal residual disease").

3. To determine the immunocompetence of patients with malignant melanoma and any correlation with prognosis.

4. To determine the influence of chemotherapy and chemoimmunotherapy upon the immunocompetence of these patients with malignant melanoma.

TECHNICAL APPROACH

There will be a separate stratification for patients according to localized and regional disease. For patients with localized disease, sufficient patients will be entered to detect as statistically significant a 20% difference in recurrence rates (significance level 5%, power 80%). For patients with regional metastases, sufficient patients will be entered to detect as significant a 20% improvement in the recurrence rate.

SWOG 7521 (continued)

Therapy will be administered according to the schema outlined in the study protocol.

PROGRESS

New study. No progress to date.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy, Splenectomy with or without Immunotherapy in the Treatment of Chronic Myelogenous Leukemia.

WORK UNIT NO.: SWOG 7522

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To study the effects of chemotherapy, splenectomy and/or immunotherapy on leukemic cytogenetics, immune status, appearance of blastic transformation and any influence in overall survival.

a. To treat and control the early benign phase of chronic myelogenous leukemia with Cytoxan, Cytosine Arabinoside, Vincristine and Prednisone and to study the influence of chemotherapy on bone marrow morphology, cytogenetics and leukocyte alkaline phosphatase.

b. To study nonspecific cell mediated immunity prior to and following therapy.

c. To determine if immunotherapy with BCG will augment general immunocompetence of CML patients.

d. To remove extra tumor burden, avoid possible complication of splenic infarction and hypersplenism through surgical splenectomy.

TECHNICAL APPROACH

To detect whether or not there has been a 20% decrease in the number of patients dying in three years requires 33 patients in each group. Hence among the group of patients receiving splenectomy, at least 33 patients will be randomized to each treatment for a total of 66 patients.

Therapy will conform with the schema outlined in the study protocol.

PROGRESS

There have been no patient registrations on this study.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Methotrexate and MeCCNU in Large Cell and Adenocarcinoma of the Lung.

WORK UNIT NO.: SWOG 7523

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To determine the effectiveness of the combination of Methotrexate and Methyl CCNU for the treatment of large cell undifferentiated and adenocarcinoma of the lung.

TECHNICAL APPROACH

Approximately 100 patients will be entered into this study. Therapy will be given in accordance with the schema outlined in the study protocol.

PROGRESS

Two patients have been registered in this study; however, no data are available at this time.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Chemotherapy in Stages II and IV Ovarian and Endometrial Cancer.

WORK UNIT NO.: SWOG 7524

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To compare the effectiveness of chemotherapy alone vs. chemoimmunotherapy for remission induction in patients with Stage II and IV ovarian and endometrial carcinoma who had had no previous cytotoxic chemotherapy.

2. To test the effectiveness of continued chemoimmunotherapy vs. chemotherapy in maintaining complete remission achieved during the initial 12-month induction therapy.

3. To rest the effectiveness of continued chemoimmunotherapy vs. chemotherapy in inducing complete remissions or maintaining partial remissions in patients with occult disease at the time of restaging for complete response or in patients achieving only partial clinical remission during the initial 12-month induction therapy.

4. To establish baseline and serial data on immunologic status in both chemotherapy and chemoimmunotherapy groups.

5. To evaluate systematic restaging of patients judged to be in complete remission.

TECHNICAL APPROACH

In order to detect a 25% improvement for each tumor type, approximately 45 fully evaluable patients would be necessary on each of the induction treatment arms. Therapy will be according to the schema outlined in the study protocol.

PROGRESS

This is a new study; no progress.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Treatment of Patients for Early Testicular Cancer with Irradiation and Chemotherapy with Vinblastine and Bleomycin.

WORK UNIT NO.: SWOG 7525

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To determine if a combination of irradiation and chemotherapy can improve the 2 year disease free interval and 5 year survival in certain morphologic subtypes of Ib and II nonseminomatous testicular tumors.

2. To determine which sequence of irradiation and chemotherapy more favorably influences remission maintenance, survival and possibly cure. In part, this will be done by compression of the AFIP classification into a more therapeutically workable classification which excludes pure seminomas and choriocarcinomas.

TECHNICAL APPROACH

Approximately 85 patients per year can be entered onto this study. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

This study was opened recently and no patients have been randomized.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Immune Evaluation of Lymphoma in Unmaintained Remission.

WORK UNIT NO.: SWOG 7580

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

1. To evaluate the immune status of patients with lymphoma who have been "successfully" treated and are in remission without therapy.

2. To correlate the presence of immune deficits with histologic type of lymphoma, pathologic stage, types of therapy and interval since therapy.

3. To correlate the immunologic profile with long term follow-up of patients in terms of disease relapse, second malignancy and duration of survival.

TECHNICAL APPROACH

Approximately 100-125 patients will be entered into the study. Therapy will conform with the schema outlined in the study protocol.

PROGRESS

This is a new study; no patients have been registered.

Status: Ongoing.

DEPARTMENT OF THE ARMY
Brooke Army Medical Center
Fort Sam Houston, Texas 78234
CLINICAL INVESTIGATION SERVICE

INVESTIGATION PROJECT RESUME

TITLE: Effect of Schedule of Activity of 5-Azacytidine in Acute Leukemia.

WORK UNIT NO.: SWOG 7603

PRINCIPAL INVESTIGATOR: Joseph D. McCracken, M.D., LTC, MC

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To compare the activity and toxicity of single dose vs. continuous 5-day infusions of 5-Azacytidine in patients with acute leukemia.

TECHNICAL APPROACH

At least 20 evaluable patients will be required in each group. Therapy will be administered according to the schema outlined in the study protocol.

PROGRESS

This is a new study. There have been no patient registrations.

Status: Ongoing.

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